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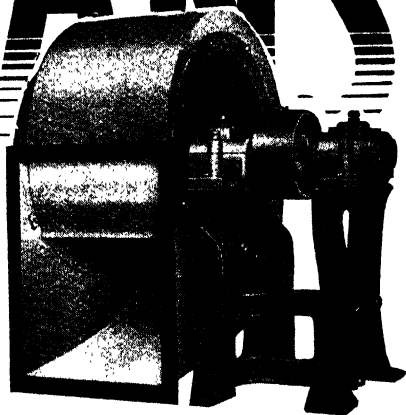
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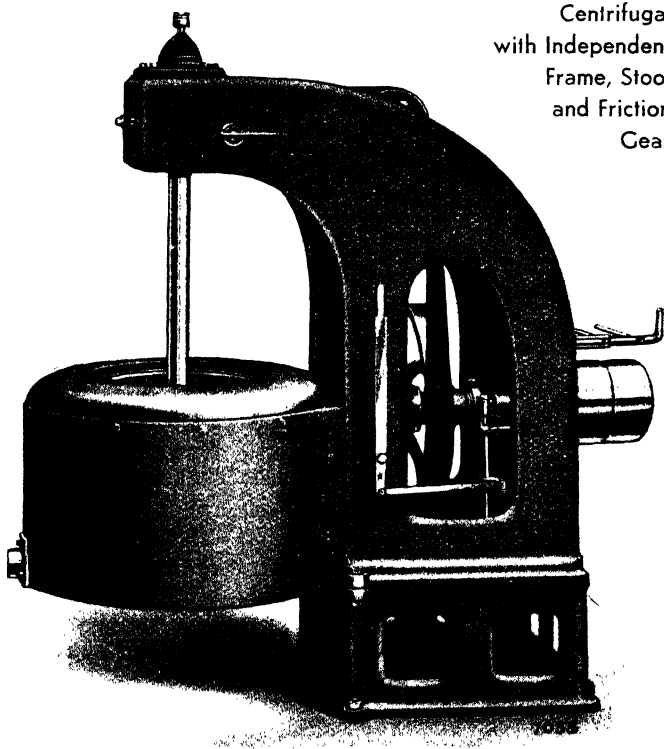
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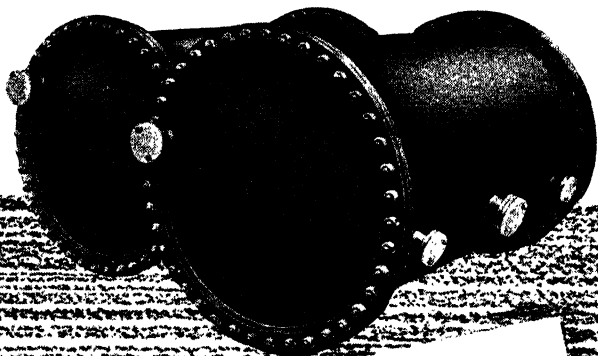
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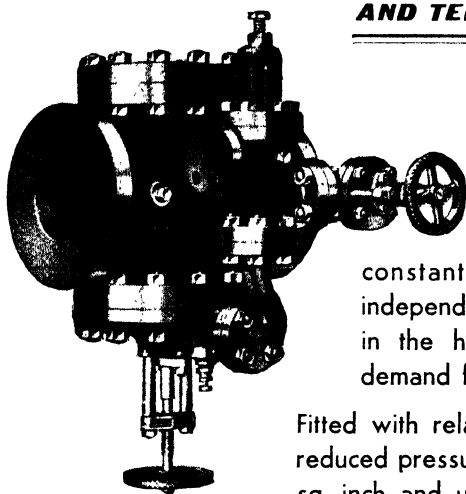
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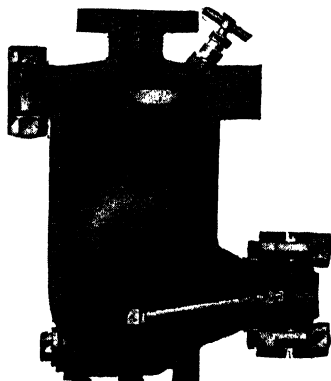
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ANNUAL REPORTS ON THE PROGRESS OF CHEMISTRY.

RADIOACTIVITY AND SUB-ATOMIC PHENOMENA.

1. INTRODUCTION AND SUMMARY.

THESE Reports do not represent an attempt at a condensed, and at the same time complete account of the advances made in nuclear physics during the current year. They are brief summaries of the most important papers which have appeared, the criterion of importance being set by the Reporters in an arbitrary manner.

It is proposed to provide next year an article on nuclear theory, so that, for the present, attention will be confined to results of a more empirical nature.

The "Mesotron."—From a fundamental point of view there is no doubt that greatest interest is centred round a growing belief in the existence of a new particle of matter, which must be regarded as fundamental in the same sense as the proton, neutron, and the electrons. In the literature this particle has been called by various names, but it seems generally agreed now that it shall be termed the "mesotron" (*i.e.*, "intermediate" particle). This particle, first suggested theoretically by H. Yukawa, has been observed only in the cosmic radiation. Theory indicates that the large penetrating power of some components of the cosmic radiation is not compatible with the properties of a particle such as the electron. On the other hand, great confidence in the theory has arisen from its success in explaining the production of cosmic ray "showers," which are assumed to arise from a cascade process of production of pairs of electrons.

It is possible, however, to account for the great penetrating power of the anomalous component of the cosmic rays by assuming it to consist of particles of mass intermediate between that of the proton and the electron. Such particles should lose energy by the production of radiation in passing through matter at a smaller rate than electrons, but, on the other hand, they should produce a detectably greater ionisation per unit path when they are moving slowly, *i.e.*, with energies of 10 m.v. or less. Photographs of such

particles have been obtained by various workers, notably by E. J. Williams. The mass of the particle determined from penetration observations, and from the ionisation near the end of the path, lies between 10 and 200 times the electron mass, with a probability that this ratio lies around 150.

Attempts have been made in the past to explain the attractive force between proton and neutron in the nucleus in terms of an exchange of charge between these particles. The assumption that this exchange takes place as a result of a virtual emission of an electron did not meet with much success. However, the new particle has proved extremely promising in this sphere, for its greater mass, and its higher spin of unity, enable a comprehensive treatment of nuclear forces to be developed.

In view of the fundamental importance of the new particle, a special article has been contributed by Professor R. Peierls, and forms the second section of this Report. A more condensed account is given by P. M. S. Blackett.¹

Technical.—Technical advances made in the sphere of atomic physics have been in the direction of improvement of existing methods rather than the development of new ones. This is particularly so in the production of high-speed ions for nuclear studies. Methods of direct acceleration of particles by high voltages have been improved, mainly by the extension of the multiplication circuit to give 2 m.v. by Messrs. Philips of Eindhoven, and by the still further development of the electrostatic belt generator working under pressure. Thus, D. B. Parkinson, R. G. Herb, E. J. Bernet, and J. L. McKibben^{1a} have given a detailed account of an apparatus producing small beams of ions with energies as great as 2.4 m.v., and W. H. Wells² has reported the progress made with the very large apparatus constructed by the Westinghouse Co., which should produce at least 5 m.v. H. A. Bethe and M. E. Rose³ and M. E. Rose⁴ have shown that the maximum energy of the particles obtained from the cyclotron is limited by loss of resonance with the electric field, owing to the relativistic increase of mass. They showed that to maintain resonance at high energies, the magnetic field of the cyclotron must increase with the radius of curvature of the paths of the ions, and that this is not compatible with focusing conditions. J. Churgin⁵ and R. R. Wilson⁶ also have discussed

¹ *Nature*, 1938, **142**, 692.

^{1a} *Physical Rev.*, 1938, **53**, 642.

² *Bull. Amer. Physical Soc.*, 1938, **13**, No. 7, 15.

³ *Physical Rev.*, 1937, **52**, 1254.

⁴ *Ibid.*, 1938, **53**, 352.

⁵ *Compt. rend. Acad. Sci. U.R.S.S.*, 1938, **19**, 237.

⁶ *Physical Rev.*, 1938, **53**, 408.

the stability of ionic orbits in the cyclotron, and recent (unpublished) considerations have indicated that by increasing the radio-frequency power, and hence the D voltage, the production of ions of energies as great as 50 m.v. or more should be possible. It has been pointed out by L. H. Thomas ⁷ that if a cylindrical variation of the magnetic field, with period $\pi/2$, be superimposed upon a magnetic field increasing from the centre outwards, stable orbits may be obtained and resonance preserved. L. I. Schiff ⁸ has shown that a cylindrical periodicity of $2\pi/3$ has some advantages, in that the amplitude of the variations required to produce focusing is less. These variations in the magnetic field are combined with a corresponding modification in the electric field, i.e., in the latter case the D -shaped electrodes are replaced by "triant" provided with three-phase power. Thus it becomes possible that the energies of particles available for nuclear studies may be increased very much in the future by the building of still larger cyclotrons.

R. R. Wilson ⁹ has shown that the currents actually circulating in the cyclotron, and which may be utilised to strike internal targets, may be of the order of milliamperes. Very powerful sources indeed of artificial radioactive elements have been prepared by using these internal targets. It is evident that the cyclotron is by far the most powerful accelerating system so far produced.

Nuclear Isomerism and Element No. 43.—Considerable advance in knowledge of isomeric nuclei has been gained during the present year, and information on some of the work is given in the section of the Report contributed by Dr. P. B. Moon.

Isomeric nuclei are atomic species with identical atomic charges and mass numbers, but with differing energy states, the state of higher energy being "metastable" in the sense that the transition to the lower state is sufficiently delayed for the higher energy state to have an appreciable lifetime. Recent discussion of the problem of nuclear isomerism has been given by N. Feather and E. Bretscher ¹⁰ and W. Bothe.¹¹ Feather and Bretscher have discussed the isomerism of $U-X_2$ and $U-Z$, in the natural disintegration of uranium. They concluded that the $U-Z$ is formed from $U-X_2$ by a (β — γ) branching in the ratio 665 : 1. A level scheme is proposed to account for the facts on the basis of C. F. von Weizsäcker's hypothesis ¹² that for small energy differences the γ -transition between

⁷ *Physical Rev.*, 1938, **54**, 580.

⁸ *Ibid.*, p. 1114.

⁹ *Ibid.*, pp. 240, 1031.

¹⁰ *Proc. Roy. Soc.*, 1938, **A**, **165**, 530.

¹¹ *Nuovo Cim.*, 1937, **14**, 501.

¹² See *Ann. Reports*, 1937, **34**, 21.

the isomers may be inhibited by a large difference in angular momentum. However, M. H. Hebb and G. S. Uhlenbeck¹³ have shown that these conditions may lead to a considerable internal conversion, so that the transition should lead more often to emission of a conversion electron than a γ -ray. At the same time, the life-time of the metastable isomeric state will be much reduced.

B. Pontecorvo¹⁴ has shown that the isomeric nucleus, ^{105}Rh , of greater energy emits a line of β -rays corresponding to the internal conversion of the γ -radiation. E. Segrè and G. T. Seaborg¹⁵ have shown that bombardment of molybdenum with deuterons, or slow neutrons, gives an active molybdenum isotope of half-life 65 hours, which decays by β -emission to a second radioactive element which emits only a line spectrum of β -rays. Chemical separation shows that this is an element of atomic number 43. It is shown both by absorption methods and by use of a magnetic spectrograph that the electrons emitted have energy of about 110 k.v., corresponding to the internal conversion of a γ -ray of 130 k.v. energy.¹⁶ Some X-rays are emitted also, identified by absorption observations in neighbouring elements as the K_α radiation from element 43. Some γ -rays are observed. The simplest assumption to account for these observations is that the activity is due to an isomeric form of element 43, which decays to a more stable form by internal conversion, and by emission of γ -rays, with a half-life of 6 hours. P. Abelson¹⁷ has since obtained X-ray spectra giving confirmation of these conclusions, using intense sources prepared in the Berkeley cyclotron. This is probably the first reliable evidence of the existence of an element of atomic number 43.

M. L. Pool and L. L. Quill¹⁸ have suggested that ^{159}Gd , which gives β -decay periods of 3.5 minutes and 17 hours, and ^{175}Yb (2.1 hours, and 14 hours) are further cases of nuclear isomerism. A. C. G. Mitchell and L. M. Langer¹⁹ have shown that the capture of slow neutrons by ^{115}In leads to the formation of two isomeric forms of ^{116}In , one of period 13 secs. and the other 54 mins. A γ -ray is associated with the decay of the latter but not with the former period. The branching ratio (13 secs. : 54 mins.) in formation is independent of the method of excitation, and is 1.12 ± 0.06 , and a level scheme can be prepared which will account for all the

¹³ *Physica*, 1938, **5**, 605.

¹⁴ *Physical Rev.*, 1938, **54**, 542.

¹⁵ *Ibid.*, p. 772.

¹⁶ Cf. D. C. Kalbfell, *Bull. Amer. Physical Soc.*, 1938, **13**, No. 6; *Physical Rev.*, 1938, **54**, 543.

¹⁷ Unpublished.

¹⁸ *Physical Rev.*, 1938, **53**, 437.

¹⁹ *Ibid.*, p. 505.

observed facts. M. L. Pool²⁰ also has given evidence for the existence of isomeric pairs of radio-iridium. M. L. Pool and E. C. Campbell²¹ have discussed the isomerism of ^{106}Ag , 24.5-min. radio-isotope, and ^{106}Ag , 8.2-day ground state. The idea of nuclear isomerism is of great importance, and it is likely to lead to considerable advances in the understanding of nuclear-energy states.

Radioactive Decay by K-Electron Capture.—A number of striking examples have been recorded of transformations of positron-emitting bodies by the capture of electrons from the *K*-shells of the elements concerned. M. L. Pool and E. C. Campbell²¹ have investigated the decay of the isomeric ^{106}Ag nucleus of 8.2 hours half-life, and find that the relative probabilities of *K*-electron capture, negative β -emission, and positive β -emission are in the ratio 640:40:1. E. J. Williams and E. Pickup²² showed that *K*-electron capture in the decay of a radio-element formed from titanium by bombardment with fast deuterons is 1000 times that of the alternative process of positron emission. L. H. Rumbaugh, L. R. Hafstad, and R. B. Roberts²³ give evidence that ^7Be decays to ^7Li by *K*-electron capture. L. Alvarez²⁴ has discussed critically the fact that evidence of emission of *K*-radiation is no real evidence alone of *K*-electron capture by a radioactive nucleus, for this may arise from internal conversion of γ -rays. It is necessary to prove that a nucleus of charge *Z* is transformed into one of (*Z*−1), and that the characteristic radiation of (*Z*−1) is emitted after the process. ^{67}Ga , formed by deuteron or α -particle bombardment of zinc, emits *X*-rays, electrons, and γ -rays. The electrons are identified by absorption and magnetic spectrographic methods as a line spectrum with lines of 90 and 99 k.v., corresponding with the *K*- and *L*-conversion of a 100 k.v. line. The *X*-radiation is identified as *Zn-K_a* and *-K_β*. Absorption of the γ -rays in lead and copper indicates an energy of 0.2—0.3 m.v. All the data are in accord with the view that ^{67}Ga is transformed into ^{67}Zn by electron capture, and that this ^{67}Zn then emits a *K-X*-ray quantum in half the cases. The excited state of ^{67}Zn then emits either a 100 k.v. or a 0.2—0.3 m.v. γ -ray quantum or both, the 100 k.v. line being strongly internally converted. Finally, another quantum of *Zn-K* radiation is emitted in about half the cases (Auger coefficient 0.5). Similarly, the same author²⁵ has discussed electron capture in the transformation of ^{22}Na into ^{22}Ne , of ^7Be into ^7Li , of a vanadium radio-isotope, and other cases.

²⁰ *Physical Rev.*, 1938, **53**, 611.

²² *Nature*, 1938, **141**, 199.

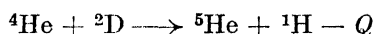
²⁴ *Ibid.*, **53**, 606.

²¹ *Ibid.*, p. 272.

²³ *Physical Rev.*, 1938, **54**, 657.

²⁵ *Ibid.*, **54**, 486.

Existence of ${}^5\text{He}$.—F. Joliot and I. Zlotowski²⁶ have described a method for identifying particles produced in nuclear transformations by passing them through a magnetic field of 16,000 Gauss produced by means of coils of wire carrying 6000 ampères, placed around a Wilson expansion chamber. The tracks of heavy particles are thus curved. Further, they give evidence²⁷ for the formation of a stable isotope of helium of mass 5, through collision between α -particles and deuterons. Examination of the particles emitted from a thin film of heavy paraffin, bombarded with polonium α -particles, showed that they consisted of deuterium and hydrogen particles in the proportion 3 : 2. The energy of the deuterons is in accord with the assumption that they are elastically projected in the collision, but the energy of the protons is 0.5 m.v. greater than that of projected protons. The α -particles have not sufficient energy to break up the deuterium nucleus, so the only possible reaction to account for the production of the protons appears to be



where Q is 0.1—0.3 m.v. The mass of the ${}^5\text{He}$ atom can be calculated from this equation and is 5.0106 ± 0.0005 , and this should be a stable species. On the other hand, H. Staub and W. Stephens²⁸ find, in agreement with J. H. Williams, W. G. Shepherd and R. D. Haxby,²⁹ that a group of α -particles of range 7.6 cm. occurs during the reaction of deuterons with ${}^7\text{Li}$. It is assumed that this arises from the reaction ${}^7\text{Li}({}^2\text{D}, {}^4\text{He}){}^5\text{He}$, and this leads to the conclusion that ${}^5\text{He}$ is unstable by 0.8 m.v. The same authors claim to have found a group of neutrons corresponding in energy to the break up of such an unstable ${}^5\text{He}$.

Helium of mass 5 is not known to occur in natural sources of the gas.

Existence of ${}^3\text{H}$.—R. Sherr, L. Smith, and W. Bleakney³⁰ have used the Hertz diffusion method to concentrate any ${}^3\text{H}$ which may be present in water. They find no evidence for a concentration in excess of one part in 10^{12} of ordinary hydrogen. On the other hand, E. Hudspeth and T. W. Bonner³¹ were able to determine the mean range for the ${}^3\text{H}$ particles emitted in the reaction ${}^2\text{H}({}^2\text{D}, p){}^3\text{H}$, indicating that ${}^3\text{H}$ must be stable during the time required for the particles to traverse the chamber.

Stability of ${}^8\text{Be}$.—A number of nuclear reactions have been studied in past years which have led to the formation of an atomic species ${}^8\text{Be}$. This isotope is not known in Nature, though the mass cal-

²⁶ *J. Phys. Radium*, 1938, **9**, 593.

²⁷ *Ibid.*, p. 403.

²⁸ *Physical Rev.*, 1938, **54**, 236.

²⁹ *Ibid.*, 1937, **51**, 888.

³⁰ *Ibid.*, 1938, **54**, 388.

³¹ *Ibid.*, p. 308.

culated from the reactions indicated that it should be stable by about 0.2 m.v. Further information concerning this isotope has accumulated during the current year. O. Laaff³² claims, on the basis of counting experiments in which he detected the simultaneous entry of two α -particles into his chamber, that ^8Be produced in the process $^{11}\text{B}(p, \alpha)^8\text{Be}$, is unstable, and breaks up into two α -particles with the emission of 0.2 m.v. of energy.

E. Glückauf and F. A. Paneth³³ have shown that the photo-disintegration of ^9Be by γ -radiation from radium leads to the production of measurable quantities of helium, the quantity formed being in accord with the assumption that the reaction leads to the formation of two α -particles and a neutron, rather than of ^8Be and a neutron. F. Kirchner, O. Laaff, and H. Neuert,³⁴ using the method of O. Laaff, have reported similar results, showing that ^8Be is unstable by between 40 and 120 k.v.

The most precise measurement of the mass of ^8Be reported so far is due to S. K. Allison, E. R. Graves, L. S. Skaggs, and W. M. Smith,³⁵ who have determined the energy of the reaction $^9\text{Be}(p, D)^8\text{Be}$ to be 0.562 ± 0.006 m.v. This is an absolute determination based on the electrostatic deflection of the deuterons, and it leads to a mass of 8.00739, which is stable with respect to α -particle disintegration by 0.31 ± 0.06 m.v.

It is seen that there is not yet sufficient evidence to reach a definite conclusion whether ^8Be is a stable atomic species, or whether it breaks up spontaneously into two α -particles, but the balance of evidence is in favour of stability.

Trans-uranium Elements.—In recent years considerable attention has been given to the possibility of the formation of elements of atomic number greater than 92 (uranium) by bombarding uranium and thorium with neutrons.³⁶ A number of different β -active bodies were found, with chemical properties compatible with those to be expected of chemical elements beyond uranium. Finally, O. Hahn and F. Strassmann^{37a} showed that isotopes of barium (atomic number 56) were produced as a consequence of the bombardment of uranium with neutrons. L. Meitner and O. R. Frisch^{37b} interpret this as indicating that the assumption of the formation of trans-

³² *Ann. Physik*, 1938, **32**, 743.

³³ *Proc. Roy. Soc.*, 1938, **A**, **165**, 229.

³⁴ *Physical Rev.*, 1938, **53**, 794.

³⁵ *Bull. Amer. Physical Soc.*, 1938, **13**, No. 7, 14.

³⁶ L. Meitner, F. Strassmann, and O. Hahn, *Z. Physik*, 1938, **109**, 538. In this paper three isomeric ^{229}Ra nuclei and three ^{229}Ac nuclei are reported; cf. (Mme) I. Curie and P. Savitch, *J. Phys. Radium*, 1937, **8**, 385; *Compt. rend.*, 1938, **206**, 1643.

^{37a} *Naturwiss.*, 1939, **27**, 11.

^{37b} *Nature*, 1939, **143**, 240.

uranium elements is false, and that one must conclude that a uranium nucleus becomes unstable when a neutron is captured, and breaks up into isotopes of two elements of much lower atomic number (*e.g.*, if one of these is $_{56}\text{Ba}$, the other must be $_{36}\text{Kr}$). Either or both of these may be radioactive, and may decay by one or more β -transformations to a stable isotope of another element. The energy available in the whole transformation process may be as great as 200 m.v. We understand (unpublished) that F. Joliot and E. Fermi each independently have reached the same conclusions, and that the recoiling fragments of the uranium nucleus have been detected and identified.

It appears, therefore, that there is no evidence as yet that radioactive elements beyond uranium can be formed in transformation of heavy elements by neutrons, and that previous assumptions that these elements exist are erroneous.

Natural Radioactivity.—Advances in the field of natural radioactivity have not been marked in 1938. A. Bramley and A. K. Brewer³⁸ have remeasured the radioactivity of potassium, and when this is corrected for the abundance of the radioactive isotope ^{40}K , they find for the half-life a value of $(14.2 \pm 3) \times 10^8$ years. C. W. Bennett³⁹ has photographed in the cloud chamber the tracks of internal conversion electrons corresponding with the energy differences between the two observed groups of α -particles from actinium, and S. P. Choong and J. Surugue⁴⁰ have obtained information about the γ -rays from various products of actinium active-deposit.

T. R. Wilkins and A. J. Dempster⁴¹ have deposited separated isotopes of samarium upon a photographic plate in a mass-spectrograph, and have shown that, after it has been left for several months and then developed, tracks of α -particles appear in the emulsion only beneath the line corresponding to the isotope ^{148}Sa . The apparent half-life of 1.2×10^{12} years obtained by G. von Hevesy and M. Pahl⁴² must therefore be reduced by a factor of 7, since the abundance of ^{148}Sa is 14% of the whole.

It has been shown by H. Suess⁴³ that the radioactivity of potassium in minerals may be used to determine the age of the materials, and O. Hahn and E. Walbig⁴⁴ point out that the geological age of rubidium-bearing minerals may be found from mass-spectroscopic

³⁸ *Physical Rev.*, 1938, **53**, 502.

³⁹ *Proc. Camb. Phil. Soc.*, 1938, **34**, 282.

⁴⁰ *J. Phys. Radium*, 1938, **9**, 437.

⁴¹ *Physical Rev.*, 1938, **54**, 315.

⁴² *Z. physikal. Chem.*, 1934, **A**, **169**, 147.

⁴³ *Naturwiss.*, 1938, **26**, 411.

⁴⁴ *Z. anorg. Chem.*, 1938, **236**, 78.

determinations of the product of the disintegration of ^{87}Rh , viz., ^{87}Sr . Measurements of this nature are reported by A. K. Brewer.⁴⁵

Atom Building in the Interior of Stars.—It is natural to assume that the chemical elements have been formed in cosmological processes from hydrogen. H. A. Bethe and C. L. Critchfield⁴⁶ have discussed the probability of the simplest of the building processes, viz., the formation of deuterium by the combination of two hydrogen atoms. Fermi's theory is used in calculating the positron emission of the process $\text{H} + \text{H} \longrightarrow \text{D} + e^+$. They show that at the centre of the sun the energy evolution by this process should amount to about 2 ergs per g. per sec., and this alone is almost sufficient to account for the whole observed evolution of energy. C. F. von Weizsäcker⁴⁷ has shown that evolution of energy can only be expected in stellar interiors from reactions involving light nuclei, and he has discussed the conditions necessary for the formation of all elements in comparable amount. G. Gamow⁴⁸ gives a relation between the features of star distribution along the main sequence and the proton-proton reaction.

Transformations Produced by Proton Bombardment.—An interesting feature of the experiments upon the bombardment of elements by fast particles is the observation that protons of high energy are able to enter nuclei very readily and eject neutrons. These reactions have been studied in greatest detail by workers in Rochester. Thus, L. A. Du Bridge⁴⁹ reports that the reactions produced are almost always of the $(p-n)$ type, though a reaction of the $(p-p)$ type leading to formation of a radioactive isomeric state of ^{115}In has been found. Over thirty $(p-n)$ reactions leading to radioactive isotopes already formed in other ways have been found, and twenty reactions are reported leading to new active isotopes. Definite effects are produced by 6.5 m.v. protons in elements as heavy as osmium, while there is some evidence for an effect produced in thorium, though most elements heavier than tellurium show no effect.

Nuclear Physics in Biology and Medicine.—The study of nuclear physics since 1934 has shown that practically every element in the periodic table may be rendered radioactive, and, during the past year a great deal of work has been done, notably by G. von Hevesy, upon the use of atoms, "labelled" by the presence of radioactive isotopes, to elucidate some of the complicated chemical processes going on in biological material. The most recent authoritative

⁴⁵ *J. Amer. Chem. Soc.*, 1938, **60**, 691.

⁴⁶ *Physical Rev.*, 1938, **54**, 248.

⁴⁷ *Physikal. Z.*, 1938, **39**, 633.

⁴⁸ *Physical Rev.*, 1938, **53**, 907

⁴⁹ *Bull. Amer. Physical Soc.*, 1938, **13**, No. 7, 19.

account of such work has been published by J. H. Lawrence,⁵⁰ a less recent article being that by G. von Hevesy.⁵¹ Full references will be found in these papers. As radioactive isotopes of all the biologically important elements are now available in quantity wherever a cyclotron of sufficient size is installed, great advances in this powerful method of attack are to be expected in the near future. In medicine, radio-sodium, and particularly radio-phosphorus, promise to be of use in the treatment of certain diseases, and the selective deposition of elements in tissues (phosphorus in bone, iodine in thyroid, etc.) introduces a new method of selective irradiation. Laboratory and clinical work on the selective action of neutrons in the destruction of neoplastic tissues, and in the treatment of malignant growths, is being carried out in a number of centres.⁵²

M. L. O.

2. THE MESOTRON.

During the last two years, convincing evidence has been found in favour of the suggestion that there exists, in cosmic rays, a hitherto unknown charged particle of a mass intermediate between those of the electron and the proton. For the name of this particle, "mesotron" now seems to be agreed upon, but in earlier papers one finds the names "U-particle," "heavy electron," "Yukon," "barytron," and "meson."

For a convincing proof one would have to give a detailed analysis of cosmic-ray phenomena,¹ but we shall outline the type of experiment which serves as evidence for each of its main properties.

The mesotron carries one positive or negative electronic charge. This can be deduced from its ionising power. The rate of production of ions on passage through matter is governed by collisions that do not involve close approach; it depends, therefore, not on the structure of the particle, but only on its charge and velocity, and is practically independent of the latter provided the particle has nearly the velocity of light. Now, it is known that the density of ions along the cloud-chamber tracks of all fast cosmic-ray particles is equal to that produced by a fast electron. Hence, if any of these tracks belong to the new particle, its charge must, within the limits of error, be equal to the electronic charge. Since it is unlikely to differ from it by a small fraction, it is reasonably certain that it is just one electronic charge. That there are positive as well as nega-

⁵⁰ "Handbook of Physical Therapy," American Medical Association, 1938.

⁵¹ *Nuovo Cim.*, New Series, Anno 15, no. 5, 279.

⁵² See J. H. Lawrence, *op. cit.*

¹ H. Euler and W. Heisenberg, *Ergebn. exakt. Naturwiss.*, 1938, 17, 1.

tive mesotrons follows from the fact ² that one knows the numbers and behaviour of positive and negative cosmic-ray particles to be very nearly the same.

The mesotron is much heavier than the electron. This was in the first instance deduced from its penetrating power, the property which led to its discovery. The data on the passage of cosmic rays through air and other materials, which were referred to in last year's Report ³ and have since been extended,⁴ show that a part of cosmic-ray particles, predominant at energies above about 2×10^8 volts, lose energy less rapidly and produce fewer showers than electrons ought to do on the quantum theory.⁵ This discrepancy cannot be due to a failure of the theory, since a fraction of the observed particles show a behaviour in accord with the theory for electrons. This suggested that the remaining particles were not electrons but new particles of greater penetrating power. The energy loss of fast electrons is, on the quantum theory, mainly due to the emission of radiation in passing through atoms, and that due to this cause is, except in very heavy elements, proportional to e^4/m^2 , e being the charge and m the mass. This formula is likely to hold for any new kind of particle as well, since again the main contribution is from collisions not involving close approach, and therefore the structure of the particle is unimportant. Since the charge of the new particle cannot be appreciably smaller than that of the electron, its mass must be greater, in order to explain its smaller energy loss.

The mesotron is lighter than the proton. We have seen that the ionisation depends on the velocity as well as on the charge, and once the velocity of the particle is appreciably less than that of light, *i.e.*, its kinetic energy is less than the relativistic rest energy mc^2 (c = light velocity), it produces noticeably more ions than a fast particle. Now one knows the distribution of momenta of particles in cosmic rays from magnetic-deflection measurements in a cloud chamber,² and if many of them were protons, one could estimate the chance of photographing them while they have a momentum less than Mc (M being the proton mass) and produce more ions on their track than fast particles. Actually, far fewer such dense tracks have been observed, and this proves that

² P. M. S. Blackett, *Proc. Roy. Soc.*, 1937, *A*, **159**, 1.

³ *Ann. Reports*, 1937, **34**, 26.

⁴ *E.g.*, P. M. S. Blackett and J. G. Wilson, *Proc. Roy. Soc.*, 1937, *A*, **160**, 306; P. M. S. Blackett, *ibid.*, 1938, **165**, 11; S. H. Neddermeyer and C. D. Anderson, *Physical Rev.*, 1937, **51**, 884.

⁵ W. Heitler, "The Theory of Radiation," Oxford, 1936; H. J. Bhabha and W. Heitler, *Proc. Roy. Soc.*, 1937, *A*, **159**, 432; J. F. Carlson and J. K. Oppenheimer, *Physical Rev.*, 1937, **51**, 220.

particles with momenta less than Mc must still move with nearly the velocity of light, and hence they cannot have proton mass.

A few tracks have now been observed for which one knows the velocity (which is less than c), from the number of ions, and the momentum, from the deflection by a magnetic field.⁶ From velocity and momentum one can find the mass of the particle, which is in most cases between 100 and 300 times the electron mass. These photographs constitute the most direct evidence in favour of the new particle. The wide variation of the mass values is probably accounted for by the difficulties involved in determining the ion density and curvature of the tracks, but the possibility is not ruled out that the mass is not the same for all these particles. The best estimate on the present evidence is in the neighbourhood of 150 electron masses.

The mesotron is not stable, but undergoes a radioactive decay. This idea, which was first suggested by Yukawa from the theory discussed on p. 19, gave a natural explanation⁷ of the otherwise inexplicable fact⁸ that the intensity of cosmic rays which travel obliquely through the atmosphere, compared with that of the vertical ones, is weaker than could be accounted for by the absorption in air (known from the altitude dependence of the vertical rays). If the mesotron decays spontaneously, the difference may be due to the longer path, and hence longer time, of travel for oblique rays. To obtain agreement, the mean life of a mesotron at rest must then be assumed to be about 2×10^{-6} sec. (A rapidly moving mesotron seems to live longer owing to the relativity time dilatation.) One of the disintegration products must be an electron. These disintegration electrons can be distinguished from those produced by collisions of the mesotron with atoms or nuclei by comparing the electrons generated in different media by penetrating cosmic rays.¹ The number of disintegration electrons produced per unit time does not depend on the nature and density of the medium through which the rays are travelling. The data are in favour of the existence of such disintegration electrons and lead to a mean life of the same order of magnitude as the above.

The mesotron is not a part of the incident radiation reaching the earth from outside, but is generated by it in the upper atmosphere. This follows from the preceding statement about the short life of mesotrons, but there is independent evidence from the absence of a latitude effect¹ in the penetrating component of cosmic rays.

⁶ *E.g.*, E. J. Williams and E. Pickup, *Nature*, 1938, **141**, 684. For fuller references, cf. Euler and Heisenberg, *loc. cit.*, p. 7 (ref. 1).

⁷ P. M. S. Blackett, *Nature*, 1938, **142**, 692.

⁸ *E.g.*, A. Ehmert, *Z. Physik*, 1937, **106**, 751.

It is likely that the process leading to a production of mesotrons is the collision of fast electrons with atomic nuclei.

So far, we have based our Report entirely on the experimental evidence as the more conclusive proof, but it is of interest to realise that the existence of mesotrons and all the above-mentioned properties were predicted on purely theoretical grounds by H. Yukawa.⁹

Yukawa tried to develop a theory of nuclear forces. It is known from the binding energies of light nuclei and from the scattering of neutrons and protons by protons¹⁰ that the forces holding the constituents of a nucleus together are short-range forces having an appreciable action only over distances of the order of 3×10^{-13} cm. At larger distances, the forces decrease rapidly, at any rate more quickly than the inverse-square law. Yukawa tried the assumption that these forces are transmitted by a field, just as the electric force between two charges is transmitted by the electromagnetic field. This assumption is extremely plausible, since a direct action at a distance (even at a distance as small as those involved in nuclear processes) would be incompatible with the postulate of relativity. However, since the nuclear forces do not satisfy the inverse-square law, the field transmitting them must satisfy equations different from those of the electromagnetic field. In other words, the wave equation

$$\nabla^2 u - \frac{1}{c^2} \frac{\partial^2 u}{\partial t^2} = 0$$

must be replaced by another one. From general requirements of relativity, the only suitable equation appears to be

$$\nabla^2 u - k^2 u - \frac{1}{c^2} \frac{\partial^2 u}{\partial t^2} = 0$$

in which k is a constant of the dimension of an inverse length. According to this wave equation, a static central field will have a potential whose variation with the distance r is given by

$$V(r) = \text{const. } e^{-kr}/r$$

This potential gives a force of the required range if the constant k is chosen to be of the order of 3.5×10^{12} cm.⁻¹. Yukawa now remarked that in quantum theory this field must be associated with particles in the same way as the electromagnetic field is associated with light quanta. A difference is that the modified wave equation now leads to waves which are propagated, not with light velocity,

⁹ *Proc. Phys. Math. Soc. Japan*, 1935, **17**, 48; 1938, **19**, 712; H. Yukawa and S. Sakata, *ibid.*, p. 1084; H. Yukawa, S. Sakata, and M. Taketani, *ibid.*, **20**, 319.

¹⁰ Cf. H. A. Bethe and R. F. Bacher, *Rev. Mod. Physics*, 1936, **8**, 82.

but with a velocity depending on the frequency ν , and hence on the energy $h\nu$ of the associated particle in the same way as the energy and velocity of a material particle of mass $h/2\pi kc$ are connected. The field which produces the nuclear forces is the de Broglie wave field of these particles. On this theory the mass of the particle is of the order of 120 electron masses, *i.e.*, of the same order as that of the mesotron found in cosmic rays.

From the behaviour of nuclear forces in large nuclei, in which they show saturation like chemical valency forces, one can conclude that the nuclear forces must be of the type of exchange forces, just as one now knows the chemical forces to be exchange forces between the electrons in the atoms. This feature is reproduced by the Yukawa theory if one adds the assumption that the particles associated with the wave field each carry one electronic charge.

The analogy with the electromagnetic field can be carried still further. The fact that charged particles produce electromagnetic fields is responsible for the other fact that if a charged particle moves with sufficient energy in a field of force, it can produce or absorb light quanta. Similarly, neutrons or protons which produce nuclear forces must, if they have sufficient energy, be able to produce mesotrons. Only, since the mesotron is charged, a neutron will, on emitting a negative mesotron, become a proton, whereas a proton, on emitting a negative mesotron, may turn into a neutron. Conservation of angular momentum (spin) then makes it evident that, since both neutron and proton each have a spin of half a unit ($h/2\pi$), the spin of the mesotron must be equal to zero or a whole number of units, and indeed this is an essential requirement of Yukawa's theory. There is no evidence on the spin of the mesotrons which are observed in cosmic rays, but all known facts are at least compatible with the assumption that they have integral spin and may therefore be identified with Yukawa's particle.

Yukawa further supposed that the process of a neutron turning into a proton on the emission of a negative mesotron took place in the β -decay of atomic nuclei, but that in the same elementary act the mesotron was further split into an electron and a "neutrino." The first part of this process is linked with the interaction of neutrons and protons with the mesotron field, and is therefore quantitatively connected with the nuclear forces. The second part is connected with the spontaneous disintegration of a mesotron into an electron and a neutrino, and thus the probability of the latter can be deduced from the observed constant of β -radioactivity. In this way one arrives at a mean life of $\frac{1}{2} \times 10^{-6}$ sec. for the mesotron, in satisfactory agreement (in view of the crude estimates involved in both values) with the cosmic-ray value of 2×10^{-6} , quoted above.

The detailed theory of nuclear forces was, following Yukawa, investigated by a number of authors.¹¹ Although the theory gives qualitatively the right type of force, it is unable to explain the force between like particles, for example, between two protons, which is known to be comparable to the force between neutron and proton. The proton field consists of positive mesotrons, and acts only upon neutrons, but not upon other protons. The forces between light particles could be accounted for if one assumed the existence, besides the charged mesotrons, of neutral particles of about the same mass.¹²

At present it seems likely that the spin of the mesotron is one unit. It must be an integer if one accepts Yukawa's theory, and if it were zero, this would produce repulsion between a neutron and a proton, instead of attraction, whereas values of 2 units or more would lead to theoretical difficulties in other respects.

In spite of the plausibility of this Yukawa theory and its extensions, and in spite of its success in predicting the observed properties of the mesotron, it meets with difficulties regarding the nature of the nuclear forces at very close approach. For this reason it is not, at present, possible to develop a mathematically consistent theory of the rôle of the mesotron in the nuclear interactions. One may hope, however, that by further modifications of the theory these difficulties will be overcome.

R. P.

3. NEUTRONS.

Although publications dealing with neutrons are still very numerous, the advances of the past year have consisted mainly in the refinement and extension of our information about processes already known. This seems an appropriate time at which to take stock of our knowledge, and, while concentrating attention upon the developments of the past year, the Reporter will not hesitate to refer briefly to work discussed in earlier Reports.

Production, Detection, and Properties of Free Neutrons.—Although neutrons are not known to be emitted during spontaneous radioactive change, the ejection of one or more neutrons from a nucleus bombarded with high-speed particles or with γ -rays is very common. Scores of such nuclear reactions are known, but only a few are of practical importance as neutron sources, either for convenience, high yield, freedom from other radiations, or suitability of the energy-

¹¹ H. Fröhlich, W. Heitler, and N. Kemmer, *Proc. Roy. Soc.*, 1938, **A**, 166, 154; H. J. Bhabha, *ibid.*, p. 501; N. Kemmer, *Proc. Camb. Phil. Soc.*, 1938, **34**, 354.

¹² N. Arley and W. Heitler, *Nature*, 1938, **142**, 158; N. Kemmer, *loc. cit.*

distribution of the neutrons for the experiment for which they are needed.

${}^2\text{D} + {}^2\text{D} = {}^3\text{He} + {}^1_0\text{n}$. This reaction, important for high yield and absence of γ -rays, has been further studied. E. Baldinger, P. Huber and H. Staub¹ have measured, with an ionisation chamber containing He, the number and ionising power of helium nuclei projected in elastic collisions by neutrons from a target of trideutero-phosphoric acid bombarded by deuterons of energies up to 0.13 m.v.² From the number of projected nuclei, and with a knowledge of the cross-section for scattering of neutrons by helium nuclei, the number of neutrons passing through the chamber may be calculated. From the geometry of the apparatus, the total rate of generation of neutrons may then be found; the authors' result was 1.2×10^{-7} neutron per deuteron, when referred to a target of pure deuterium and a deuteron energy of 0.1 m.v., and agrees reasonably well with those of R. B. Roberts³ and of R. Ladenburg and M. H. Kanner.^{4, 5}

It now seems certain that some of the earlier estimates of the yield of this reaction were far wrong. From the ionising power (which gives the energy) of the projected nuclei, the energy-distribution of the neutrons may be deduced. In agreement with previous work, a fairly homogeneous group of neutrons of about 2.5 m.v. was found; slower neutrons around 1 m.v. were considered to be due to scattering of these in neighbouring objects. The total energy released in the reaction, of which part goes to the ${}^3\text{He}$ nucleus, is 3.1 m.v., as against 3.4 ± 0.1 m.v. found by P. G. Kruger, W. E. Shouff, R. E. Watson, and P. W. Stallman⁶ from measurements of the projected deuteron tracks produced by these neutrons in a cloud chamber containing some deuterium. T. W. Bonner⁷ finds that the group of slower neutrons is of homogeneous energy 1.08 m.v., and ascribes them to the ${}^3\text{He}$ nucleus being left in an excited state.

${}^7\text{Li} + {}^2\text{D} = {}^8\text{Be} + {}^1_0\text{n}$. The energies of neutrons produced by this reaction have been studied by W. E. Stephens⁸ by way of helium nuclei projected by them in a cloud chamber. He reports two groups of energies, 14.01 and 11.1 m.v., corresponding with disintegration energies 15.05 ± 0.2 and 11.8 ± 0.4 m.v. The

¹ *Helv. Physica Acta*, 1938, **11**, 245.

² m.v. = million electron-volts in contexts where an energy is concerned.

³ *Physical Rev.*, 1937, **51**, 810.

⁴ *Ibid.*, **52**, 911.

⁵ For a critical summary of work up to the end of 1937 on yields from this and other reactions, see C. J. Bakker, W. de Groot, and F. M. Penning, *Nederl. Tijds. Natuurk.*, 1938, **5**, 102.

⁶ *Physical Rev.*, 1938, **53**, 1014.

⁷ *Ibid.*, p. 771.

⁸ *Ibid.*, p. 223.

group of lower energy is five times the more intense. These results were obtained with deuterons of energies up to 0.93 m.v. M. L. Pool,⁹ using 5.7 m.v. deuterons from a cyclotron, finds energies up to 20.8 m.v. in the forward direction. The angular distribution of neutrons agrees with the reaction ${}^7\text{Li} + {}^2\text{D} = {}^4\text{He} + {}^4\text{He} + {}^1n$ rather than with the production of ${}^8\text{Be}$.

${}^9\text{Be} + {}^4\text{He} = {}^{12}\text{C} + {}^1n$. The α -particle bombardment of beryllium, which for this purpose is mixed with radium or radon, is still an important source because of its small size and convenience, and is a suitable standard of comparison for the strength of any other neutron source. The number of neutrons emitted per second from 1 millicurie of radon mixed with beryllium powder is still rather uncertain, Amaldi's value of 25,000 being usually employed. The energy-distribution is complex, depending upon the energy of the bombarding α -particles, and extends up to several m.v.¹⁰

${}^2\text{D} + \gamma \longrightarrow {}^1\text{H} + {}^1n$. The irradiation of deuterium by γ -rays is useful as a source of neutrons of known energy. Since the binding energy of the deuteron is 2.2 m.v., a γ -ray of energy E gives an available energy of $(E - 2.2)$ m.v., which is shared nearly equally between the neutron and the proton.

The Detection of Neutrons.—Although no great advances in the methods of detection of neutrons have been made during the past year, a summary of the present position may be useful.

Since neutrons interact only with nuclei and not with electrons, they cannot be detected directly by the methods (ionisation chamber, cloud chamber, etc.) available for particles which ionise gases; they are detected by the ionising particles which they produce by collisions with atomic nuclei. Four cases may be distinguished :

(i) If the neutron is fast and the struck nucleus light, an *elastic* collision will project the nucleus with sufficient velocity for its ionisation to be detectable. Examples of this method have already been given.

(ii) An *inelastic* collision of a neutron (fast or slow) with a nucleus may cause a transmutation with the immediate expulsion of an ionising particle such as an α -particle or a proton. An important example is the reaction ${}^{10}\text{B} + {}^1n \longrightarrow {}^7\text{Li} + {}^4\text{He}$, which is employed in the "boron chamber"—an ionisation chamber with boron-lined walls or filled with boron trifluoride—coupled to a valve amplifier to magnify the ionisation caused by each α -particle.

(iii) A neutron-produced transmutation may yield a radioactive product whose activity, measured subsequently by any appropriate

⁹ *Physical Rev.*, 1938, **53**, 711.

¹⁰ See T. Bjerger, *Proc. Roy. Soc.*, 1938, *A*, **164**, 243.

method, gives an indirect measure of the intensity of the neutron radiation.

(iv) The nuclear transmutation and/or subsequent radioactive disintegration may be accompanied by γ -radiation. Since γ -rays themselves can be detected only indirectly, this is an insensitive means of detecting neutrons.

Mass of the Neutron.—If energy E (ergs) is required to disintegrate a particle of mass m_1 (g.) into two particles of masses m_2 and m_3 , the equivalence of mass and energy requires that $m_1 + E/c^2 = m_2 + m_3$, c being the velocity of light. If the masses are expressed on the scale $^{16}\text{O} = 16$, and the binding energy E is measured in m.v., the equation becomes $m_1 + 0.00107E = m_2 + m_3$. A determination of the energy required to disintegrate the deuteron into a neutron and a proton thus enables the mass of a neutron to be found in terms of those of the proton and the deuteron. A determination by this means, by J. Chadwick, N. Feather, and E. Bretscher leading to a value of 1.00902 was discussed in last year's Report, but it has since been pointed out ¹¹ that this value must be amended to 1.00893 if the newer data ¹² for the connection between the range and the energy of slow protons are accepted as correct. An independent determination of the binding energy of the deuteron which does not involve this range-energy relation has led to the result 1.00895.¹³

Spin of the Neutron.—J. Schwinger ¹⁴ has pointed out that experiments on the scattering of neutrons by ortho- and para-hydrogen could resolve any doubt that the spin of the neutron is $\frac{1}{2}$ (in units of $\hbar/2\pi$), and not $\frac{3}{2}$; the experiments of F. G. Brickwedde, J. R. Dunning, H. J. Hoge, and J. H. Manley ¹⁵ confirm the value $\frac{1}{2}$.

Magnetic Moment of the Neutron.—The experiments of O. R. Frisch, H. von Halban, and J. Koch, mentioned last year, have now been published in full; ¹⁶ the value of about -2 nuclear magnetons still holds.¹⁷

Collisions of Neutrons with Nuclei.—(i) *Fast neutrons* (energy ~ 1 m.v.). The usual initial process in neutron-nucleus collisions

¹¹ H. A. Bethe, *Physical Rev.*, 1938, **53**, 313.

¹² D. B. Parkinson, R. G. Herb, J. C. Bellamy, and C. M. Hudson, *ibid.*, 1937, **52**, 75.

¹³ G. Stetter and W. Jentsch, *Z. Physik*, 1938, **110**, 214.

¹⁴ *Physical Rev.*, 1937, **52**, 1076.

¹⁵ *Ibid.*, 1938, **54**, 266; cf. *Ann. Reports*, 1937, **34**, 23.

¹⁶ *Physical Rev.*, 1938, **53**, 719.

¹⁷ A nuclear magneton = Bohr magneton \times (mass of electron)/(mass of proton) = magnetic moment due to orbital motion of a proton rotating in an orbit with angular momentum $\hbar/2\pi$. The negative sign means that the directions of spin and magnetic moment are related as they would be for a rotating negative charge.

is believed to be the combination of the neutron with the nucleus and the sharing of its kinetic energy and energy of combination with all the nuclear particles. The excited nucleus may now get rid of its energy by the re-emission of a neutron (equivalent to scattering of the original neutron, elastically or inelastically according to whether it carries away the whole of the original kinetic energy or not); or by the emission of γ -radiation, so much energy being radiated that neither the neutron nor any other particle can escape from the nucleus, which therefore remains an isotope of the original nucleus; or by the emission of a charged particle (α -particle or proton). The probabilities of these competing processes will depend upon the nature of the initial nucleus and the energy of the neutron, but it is clear that for fast neutrons inelastic scattering must be much more probable than elastic scattering, which requires the whole of the excess energy to become concentrated once more on a single neutron.

It is, of course, possible that a neutron may "graze" the surface of a nucleus without "sticking" to it, and be scattered without much loss of energy. The ratio of elastic scattering to all other processes therefore measures the ratio of "non-sticking" to "sticking" collisions. D. C. Grahame and G. T. Seaborg¹⁸ find that for fast radon-beryllium neutrons and for several elements, the "sticking probability" is of the order of 0.4. A. Soltan¹⁹ also finds it to be less than unity.

*Nuclear transmutations produced by fast neutrons. 1. (n, γ) Processes.*²⁰ Although these processes are frequently reported with fast neutrons, they happen to such a remarkable extent with slow neutrons that great care must be taken to remove all possibility that they may be due to a relatively small proportion of slow neutrons produced by scattering in neighbouring bodies. Experiments believed to be free from this possibility have recently been made by E. T. Booth and C. Hurst, by H. Reddemann, and by H. von Halban and L. Kowarski, who are agreed on the existence of (n, γ) processes for fast neutrons. The last authors²¹ find that neutron-capture occurs most readily for those elements which absorb *slow* neutrons strongly—a somewhat disturbing result, since the strong capture of slow neutrons is assumed to be due to the accidental correspondence of a nuclear resonance level with the narrow band of energies in which slow neutrons can be obtained in

¹⁸ *Physical Rev.*, 1938, **53**, 795.

¹⁹ *Naturwiss.*, 1938, **26**, 124.

²⁰ The symbol (n, γ) indicates a process in which a neutron enters the nucleus and a γ -ray comes out. Similar notations will be used for other nuclear reactions.

²¹ *Nature*, 1938, **142**, 392.

large numbers; since the energies of the fast neutrons spread over a band much wider than the separation of neighbouring resonances, little selectivity as between different elements (and certainly not the same selectivity as for slow neutrons) would have been expected.

2. $(n, 2n)$ Processes. The net loss of one neutron is a common process under fast-neutron bombardment; the resulting isotope, having a greater ratio of charge to mass than the stable isotope from which it was formed, will often be positron-radioactive. The identification of ^{151}Gd , ^{163}Er , and ^{159}Dy made by this process enabled M. L. Pool and L. L. Quill²² to predict the existence of the stable isotopes ^{152}Gd , ^{164}Er , and ^{159}Dy , which have since been confirmed mass-spectrographically.²³ In this work seventeen $(n, 2n)$ reactions were found with rare-earth elements.

3. (n, p) Processes. The ejection of a proton is common with fast neutrons. If the resulting isotope is radioactive, it usually emits an electron, the original nucleus being thereby regenerated.

4. (n, α) Reactions. A number of instances are known of the ejection of an α -particle by a fast neutron.

(ii) *Slow neutrons.* Fast neutrons lose energy by scattering in passing through matter, and if the matter is rich in hydrogen and free from strongly absorbent nuclei, elastic collisions with protons rapidly reduce the neutrons to thermal velocities, though quantum restrictions as to the amounts of energy which a proton bound in a molecule can take up from a neutron hinder the establishment of thermal equilibrium, particularly at low temperatures. Two purely electrical methods of separating neutrons of defined velocities in the thermal range have recently been described,^{24, 25} and with one of them the approximately Maxwellian velocity-distribution of the "thermal" neutrons has been verified somewhat more accurately than hitherto. Neutrons of all higher energies, on their way towards thermal equilibrium, are of course also present, but most of the observed "slow neutron phenomena" seem to arise from neutrons below about 100 volts.

(n, γ) Processes with slow neutrons. The cross-sections for capture of slow neutrons by many nuclei (*e.g.*, boron, lithium, cadmium, silver, iodine, gold) reach, for certain velocities of neutrons within this range, values enormously greater than the nuclear dimensions. Considerable information as to the positions, widths, and heights of these absorption bands has been obtained by indirect methods,²⁶ but progress during the past year has been slow

²² *Physical Rev.*, 1938, **53**, 437.

²³ A. J. Dempster, *ibid.*, p. 727.

²⁴ L. W. Alvarez, *ibid.*, **54**, 609.

²⁵ G. E. F. Fertel, P. B. Moon, G. P. Thomson, and C. E. Wynn-Williams, *Nature*, 1938, **142**, 829.

²⁶ See H. A. Bethe, *Rev. Mod. Physics*, 1937, **9**, 71 (§§ 60, 61, 62).

and the subject seems to await new methods of attack. In this connection, papers by S. Nishikawa, S. Nakagawa, and I. Sumoto²⁷ and by A. E. Downing and C. D. Ellis²⁸ are of interest. These authors develop a method due originally to von Halban in which the thickness of hydrogenous material through which neutrons must pass in order that their velocities may change from one absorption band to another is used to give information about the relative positions of the two bands.

(n, α) *Processes.* The capture of slow neutrons by boron and by lithium is accompanied by the immediate emission of an α -particle, and there is good evidence that the dependence of capture cross-section upon velocity does not show the sharp resonances characteristic of the (n, γ) process but varies inversely as the neutron velocity. Details of energies involved in the reaction $^{10}\text{B} + {}^1_0\text{n} = {}^7\text{Li} + {}^4\text{He}$ are still obtained differently by different authors. The best experimental method to date seems to be that of J. C. Bower, E. Bretscher, and C. W. Gilbert,²⁹ who measure the total length of lithium and helium tracks in a cloud chamber, and fix the proportion to be assigned to each nucleus by ionisation-density measurements along the tracks. They find the lithium particle to have a range of 4.3 ± 0.2 mm. in air, and the helium particle to have one of 7.0 ± 0.3 mm. It is disappointing that there should be little agreement between these results and those of M. S. Livingston and J. G. Hoffman,³⁰ who find by an ionisation-chamber method two groups of helium particles of ranges 8.0 and 6.6 mm.

P. B. M.

4. ARTIFICIAL RADIOACTIVITY.

This section of the Report deals with the spontaneous (delayed) changes which occur in many of the nuclei produced by the bombardment of stable elements by protons, neutrons, γ -rays, etc. The year's progress in the field of artificial radioactivity is notable for two reasons. The first is that nuclear isomerism (*i.e.*, the existence of long-lived nuclei of the same mass and charge but different properties) has now been recognised in a considerable number of elements and is no longer reckoned as a rarity; the second is the experimental proof of a new type of nuclear transformation—the absorption of a K -electron into the nucleus. These advances are important, not only for their own interest, but also because they have indirectly brought into prominence the idea of competition

²⁷ *Sci. Papers Inst. Phys. Chem. Res. Tokyo*, 1937, **34**, 1.

²⁸ *Nature*, 1938, **142**, 793.

²⁹ *Proc. Camb. Phil. Soc.*, 1938, **34**, 290.

³⁰ *Physical Rev.*, 1938, **53**, 227.

between the various processes by means of which a nucleus may get rid of energy.

Types of Spontaneous Nuclear Change.—The Reporter believes that the discussion of the developments of the past year can be made both more concise and more intelligible if an account is first given of the ways in which nuclei may spontaneously lose energy at measurable times after their formation.³¹ If it be granted that nuclei are composed of neutrons and protons, two nuclei can differ only in respect of (i) charge Z (equal to the number of protons), (ii) mass-number A (equal to the number of protons + number of neutrons), and (iii) internal configuration. Differences of internal configuration will be associated with differences of internal energy, and the existence of “isomeric” nuclei having identical values of Z and A but different properties must necessarily be referred to differences of internal energy. Since a nucleus having energy greater than that of its “ground state” normally radiates that energy as a γ -ray without measurable delay, we can only explain nuclear isomers by the existence of one or more energy levels above the ground state which have a probability of γ -ray emission per unit time enormously less than usual. If this probability is zero, the isomer of higher energy will be, as regards γ -emission, completely stable; however, the most general assumption to make, and the one which fits the experimental facts, is that the radiation probability is low but finite, so that the isomer is “metastable” against γ -emission. The reason for the low radiation probability does not matter for our present purpose, but it is generally supposed, following a suggestion of C. F. von Weizsäcker,³² to arise from a large difference of nuclear spin between the states.

We now have the following four ways in which a given nucleus in a given state of energy can spontaneously change :

- | | |
|---|-----------------------------|
| 1. Electron (β -particle) emission | $Z \longrightarrow Z + 1$ |
| 2. Positron emission | } $Z \longrightarrow Z - 1$ |
| 3. Capture of K -electron | |
| 4. Emission of γ -ray | Z unchanged |

There will be a definite probability per unit time for the nucleus to change in each of these four ways; if we denote these probabilities by p_1, p_2, p_3, p_4 , the total probability of change per unit time is $P = p_1 + p_2 + p_3 + p_4$, and the number N of nuclei remaining in the original state after time t is related to the original number, N_0 , by the equation

$$N = N_0 e^{-Pt}$$

³¹ α -Radioactivity will be mentioned only incidentally, being characteristic only of very heavy nuclei.

³² *Naturwiss.*, 1936, **24**, 813; see *Ann. Reports*, 1937, **34**, 21.

Now the magnitudes of the transition probabilities p_1, p_2, p_3, p_4 , vary enormously from one nucleus to another. One or more of them may be zero,³³ the corresponding transition being energetically impossible. On the other hand, the probability of one of these processes [particularly (4), if there exists a lower state of energy with a not very different value of the nuclear spin] may be so high that the corresponding mean lifetime is a very small fraction of a second. However this may be, the wide range of possible values for the p 's usually ensures that one of the four processes has a probability much higher than the combined probabilities of the other three, so that it alone is effective. On the other hand, we shall occasionally find that the two most probable processes have comparable probabilities, so that some nuclei are transformed in one way and some in another, the "branching ratio" being the ratio of the two transition probabilities. The number of the original nuclei remaining, and hence the rate of occurrence of the two competing processes, will decrease with time with the single decay constant P . Such branching transformations, the competing processes being α - and β -emission, are already familiar among the naturally occurring unstable nuclei of high atomic number. Several examples among the artificial radio-elements will be found in Table I.

Secondary Processes.—Any single nucleus, after having changed by one of the above four processes, may or may not be completely stable. It is very commonly left in a state of energy above its ground state and emits one or more γ -rays in reaching the ground state; since it is exceptional for γ -radiation to have the low probability per unit time required to explain nuclear isomerism, such γ -radiation will usually occur immediately. It is, of course, possible that the nucleus may arrive into a state of appreciable lifetime as regards γ -radiation, or that it may undergo transformation by one or more of the other three processes; if so, we return to the starting point except that, the nucleus being now of different atomic number or different state of energy, the four transition probabilities will all be different and the type(s) and time-constant of transformation may have no similarity to those of the former nucleus. We thus have the possibility of a "chain" of spontaneous transformations; such chains are highly characteristic of natural radioactivity, but rare in the lighter elements.

More important in practice are secondary processes brought about outside the nucleus by the radiations emitted in the primary transformation, which will all decay in intensity at the same rate as the primary process. The most important of these are as follows :

- (i) If the primary process is positron emission, the annihil-

³³ For a stable nucleus in its ground state all four are, of course, zero.

TABLE I.

Half-Periods and Mass-Numbers of Radioactive Nuclei.

[illegible]

TABLE I (contd.).

[illegible]

[+ = positron emission; - = electron emission; k = electron capture;
α = α-particle emission].

* The unstable ^8Be nucleus thus formed disintegrates immediately into two α -particles.

ation of these positrons in passing through matter will give γ -radiation.

(ii) If the primary process is K -electron capture, the vacancy in the K -shell will lead to the emission of X -rays characteristic of the product element of atomic number $Z-1$.

(iii) If the primary process is γ -radiation, a line spectrum of electrons will be produced by the "internal conversion" of the γ -ray energy in the electronic structure of the emitting atom. Electrons may similarly be produced by γ -rays emitted as the nucleus "settles down" after other forms of transformation.

It will be realised that the radiations emitted as the result of spontaneous disintegration of a single variety of nucleus may be quite complex; when it is also remembered that the disintegration of a stable element by any one kind of nuclear bombardment frequently produces several nuclear varieties, the difficulty of determining the mode of transformation of certain unstable nuclei will be understood. Although some of the inferences mentioned below and included in Table I may have to be revised, it seems likely that the majority are not far wrong.

Nuclear Isomerism.—Among the instances of nuclear isomerism now recognised,³⁴ the following seem, for one reason or another, specially interesting.

Scandium. It now seems certain^{35, 36} that the positron-emitters of 52-hour and 4-hour half-periods obtained by bombarding scandium with fast neutrons are both due to ^{44}Sc . The 4-hour activity had previously been assigned to ^{43}Sc , and its production from the only stable isotope (^{45}Sc) had been taken as evidence for a $(n, 3n)$ reaction. No evidence of this type of reaction now exists. Similarly, the activity obtained by W. Gentner by irradiating scandium with energetic γ -rays must be due to the reaction $^{45}\text{Sc}(\gamma, n)^{44}\text{Sc}$ and not to $^{45}\text{Sc}(\gamma, 2n)^{43}\text{Sc}$. It seems possible that ^{46}Sc has three electron-emitting isomers of half-lives about an hour, two months,³⁷ and a year or more. Altogether there appear to be at least seven radioactive isotopes of scandium.

Rhodium. The 44-sec. and 4.2-min. electron-emitting bodies obtained by the irradiation of rhodium with slow neutrons have been shown to be ^{104}Rh isomers, produced by the reaction $^{103}\text{Rh}(n, \gamma)^{104}\text{Rh}$. B. Pontecorvo³⁸ finds evidence that the isomer of higher energy decays mainly by the emission of γ -radiation with the 4-min. period

³⁴ See Table I.

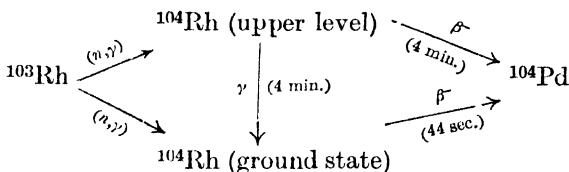
³⁵ W. E. Burcham, M. Goldhaber, and R. D. Hill, *Nature*, 1938, **141**, 510.

³⁶ J. M. Cork and R. C. Thornton, *Physical Rev.*, 1938, **53**, 866.

³⁷ This has been omitted from Table I.

³⁸ *Physical Rev.*, 1938, **54**, 542.

to the ground state, which emits β -rays and has the 44-sec. half-period, thereby becoming palladium. If such a chain reaction is taking place, the number of rays emitted in the early stages of irradiation should vary with time in a more complicated way than if a single decay process were involved. Unfortunately, the very much greater intensity of β -rays of 44-sec. period from the direct production of the ground state in the original nuclear reaction makes this verification impossible. It also seems likely that some of the nuclei in the upper state go directly by β -emission to palladium, so that we have a γ - β branching. The accompanying figure indicates the suggested processes :



The γ -rays emitted in the transition from the upper level to the ground state are not themselves observed; what are actually measured are the electrons from their internal conversion.³⁹ E. C. Crittenden and R. F. Bacher⁴⁰ report experiments supporting Pontecorvo's conclusions.

K-Electron Capture.—The possibility of this process of nuclear change was suggested by H. Yukawa and S. Sakata⁴¹ on the following lines. The emission of a positron from a nucleus may be considered as due to the simultaneous occurrence of two processes : (i) the creation of a positron-electron pair, (ii) the combination of the electron with a nuclear proton which is thereby transformed into a neutron. The emission of a positron is therefore energetically possible if the energy set free by the combination of a nuclear proton with an electron is at least equal to that required to provide the rest-energy of a positron and an electron ($2mc^2$, or about 1 m.v.). On the other hand, the capture of an orbital electron by the nucleus is energetically possible if the combination of the electron with one of the nuclear protons releases any positive amount of energy; this process is therefore energetically more probable than positron emission, and though it is geometrically less favourable because the *K*-electrons rarely come close to the nucleus, it may be expected to occur in those instances where the energy available from the change of a proton into a neutron lies between 0 and $2mc^2$, and as a branch process even when

³⁹ Theoretical reasons are given by M. H. Hebb and G. E. Uhlenbeck, *Physica*, 1938, **5**, 605.

⁴⁰ *Physical Rev.*, 1938, **54**, 862.

⁴¹ *Proc. Phys. Math. Soc. Japan*, 1935, **17**, 467; *ibid.*, 1936, **18**, 128.

the available energy is above $2mc^2$. G. J. Sizoo⁴² later showed that under certain conditions a branching between electron capture and electron emission might be expected.

A survey of the experimental evidence for electron capture, both of the Yukawa and of the Sizoo type is given by L. W. Alvarez,⁴³ who was largely responsible for establishing the existence of the phenomenon, which is usually best observed by way of the characteristic X-rays of the product element which arise from the filling of the vacancy in the *K*-shell. Alvarez showed that ^{67}Ga disintegrates with the emission of X-rays characteristic of zinc but emits no positrons. This, then, is an example of pure electron capture. The first example of positron emission—electron capture branching—is that of a zinc isotope (probably ^{65}Zn) of 8 months half-life.^{43, 44, 45} O. Oldenberg⁴⁶ showed that ^{180}Ta , obtained by irradiating tantalum with fast neutrons, decays by electron capture to ^{180}Hf . Some β -rays are also observed, and it is probable⁴³ that they also come from the ^{180}Ta nucleus, so that we have here an example of electron emission—electron capture branching. A most interesting suggestion by von Weizsäcker⁴⁷ is that the natural radioactivity of potassium is a branching reaction of this type. Since the radioactive isotope is ^{40}K , electron capture would yield ^{40}A , the production of which from potassium might explain its relatively high natural abundance. The isotope ^7Be , which may be obtained by the reactions $^6\text{Li}(\text{D}, n)^7\text{Be}$ and $^{10}\text{B}(\text{D}, \alpha)^7\text{Be}$, decays with a half-life of 43 days and emits γ -rays only. The decay process is the capture of a *K*-electron with the formation of ^7Li in an excited state, the transition to the ground state giving the observed γ -ray.⁴⁸ For other examples of electron capture, reference may be made to Alvarez's paper and to Table I.

Data concerning Stable and Radioactive Nuclei.—To the summaries referred to in last year's Report may be added an article by K. Diebner and E. Grassmann⁴⁹ surveying data obtained between 1937 and March 1938, and tables by Grégoire⁵⁰ corrected to October 1st, 1938. Table I of this Report shows in semi-graphical form the half-lives, types of disintegration, and mass numbers of radioactive nuclei up to $Z = 81$, publications available to the Reporter up to the end of 1938 being included.

Chemical Aspects.—Chemical and physicochemical methods

⁴² *Physica*, 1937, **4**, 467.

⁴³ *Physical Rev.*, 1938, **54**, 486.

⁴⁴ *Ibid.*, **53**, 946.

⁴⁵ J. J. Livingood and G. T. Seaborg, *ibid.*, **54**, 239.

⁴⁶ *Ibid.*, **53**, 35.

⁴⁷ *Physikal. Z.*, 1937, **38**, 623.

⁴⁸ R. B. Roberts, N. P. Heydenburg, and G. L. Locher, *Physical Rev.*, 1938, **53**, 1016.

⁴⁹ *Physikal. Z.*, 1938, **39**, 469.

⁵⁰ *J. Physique*, 1938, **9**, 419.

continue to be of great service. The identification of activity as belonging to a particular nucleus is rarely accepted unless it be shown that the activity is carried with the correct fraction in a chemical separation of the elements to which it might belong. The partial separation of active from inactive nuclei is of great value as a means of concentrating the activity; a recent example is the concentration of radioactive copper from a neutron-irradiated zinc solution by electrolysis with a rotating cathode.⁵¹ The concentration of radioactive gallium by extraction with ether is described by Alvarez.⁴³

An important application of a micro-chemical method is afforded by the work on the γ -ray disintegration of ^9Be .⁵² J. W. J. Fay, E. Glückauf, and F. A. Paneth⁵³ have shown that the helium content of beryls cannot be explained by the disintegration of a hypothetical ^8Be , and is probably not connected with beryllium at all.

The applications of radioactive indicators to problems in chemistry have been surprisingly few⁵⁴ in view of the fact that radioactive forms of all but two or three of the elements are known. It is true that for many elements no radio-isotope of convenient period is known, and that supplies of most of them can only be had from laboratories where a cyclotron or other powerful source of fast particles is available. In this last respect the situation will improve, and one may hope that this branch of the subject may require fuller consideration in future Reports. With this application in view, Table I has been arranged so as to emphasise the half-lives of the radioactive nuclei.

P. B. M.

P. B. MOON.

M. L. OLIPHANT.

R. PETERLS.

⁵¹ J. Steigman, *Physical Rev.*, 1938, **53**, 771.

⁵² See this Report, p. 13. ⁵³ *Proc. Roy. Soc.*, 1938, **A**, **165**, 238.

⁵⁴ But see O. Hahn, *Z. Elektrochem.*, 1938, **44**, 497; J. J. Livingood and G. T. Seaborg, *J. Amer. Chem. Soc.*, 1938, **60**, 2524. For references to biochemical applications, see this vol., pp. 15, 16, and 347.

GENERAL AND PHYSICAL CHEMISTRY.

1. INTRODUCTION.

THERE has been a growing tendency in recent Reports on General and Physical Chemistry to select a number of topics and review the progress made over two or three years in order that the treatment may be made more critical and also more useful to the non-specialist for whom the Reports are intended. In the following sections of this Report this policy has been carried even further, since there seems to be a desire for such a modification of the articles. The choice this year has been dictated partly by the state of the particular branch of physical chemistry and partly by the topics dealt with in the past two years. It is hoped that this arrangement will not curtail the scope of the Reports, the number of references quoted being nearly the same as in previous years. Again, space will not permit of a really comprehensive review, since the maximum number of papers to which reference can be made represents only 10% of the total published.

The Report is divided into four sections. The first, by G. B. B. M. Sutherland, is concerned with infra-red and Raman spectra. Here the tendency is to stress the importance of the application of these techniques to the solution of chemical problems rather than to the determination of the structure and force constants of polyatomic molecules. Within recent years there has been much discussion about the more fundamental aspects of the adsorption of gases by solids in simple and sufficiently well-defined systems. A summary and critical discussion of this subject is given by J. K. Roberts with special reference to its possible application, in due course, to the mechanism of heterogeneous catalysis. In this connection mention may be made of the second edition of N. K. Adam's well-known book on the "Physics and Chemistry of Surfaces" (Oxford), which has been brought thoroughly up-to-date. As in the first edition, the properties of the liquid-gas interface receive the greatest prominence. During the year under review E. F. Burton has produced a third edition of the "Physical Properties of Colloidal Solutions" (Longmans), and H. B. Weiser has completed Vol. III of his "Inorganic Colloid Chemistry" (Chapman and Hall, London), dealing with the colloidal salts.

The subject matter of chemical kinetics covers such a wide field that an annual report is absolutely necessary, but only a few aspects

can be treated in any one article. This year, attention has been devoted mostly to reactions connected with solids, the reason for the choice being that a summary of the present position of this, the most intractable branch of kinetics, has not been attempted recently. Two books on kinetics must be mentioned, the first by G. M. Schwab, H. S. Taylor, and R. Spence on "Catalysis from the Standpoint of Chemical Kinetics" (Macmillan), which deals with the subject in the most comprehensive manner, and the second by Farrington Daniels on "Chemical Kinetics" (Cornell University Press), who limits himself to a small number of topics which are considered from a practical standpoint.

The last section of the Report, by F. P. Bowden and J. N. Agar, is a critical discussion of the nature of electrode processes.

H. W. M.

2. SPECTROSCOPY.

This Report will be concerned entirely with the infra-red and Raman spectra of polyatomic molecules, as it is not possible to include even the briefest review of electronic spectra in the space available. In previous years¹ general surveys have been made of the principles on which the interpretation of vibration-rotation spectra are based; this year it is proposed to deal with some of the more novel applications to specific physicochemical problems. Important advances in the general theory since 1936 will be briefly noted, and the earlier tables of data on the structural constants of simple polyatomic molecules revised where necessary. It is hoped that this will round off the treatment of this branch of spectroscopy so that next year's Report may be devoted mainly to a comprehensive review of electronic spectra. A book of considerable importance which has appeared since the last Report is the supplementary volume² of Kohlrausch's "Smekal-Raman-Effekt" which, in addition to an excellent review of the developments in this field as a whole, contains references to over 1200 publications which have appeared between 1931 and the end of 1937. Tables of the actual frequencies are no longer included: for these one must refer to Landolt-Börnstein "Tabellen" or the Annual Tables of the Conseil International des Unions Scientifiques,³ neither of which unfortunately goes beyond 1935. Another publication of interest is "Spectroscopy in Science and Industry,"⁴ which is really a summary

¹ L. A. Woodward, *Ann. Reports*, 1934, **31**, 21; G. B. B. M. Sutherland, *ibid.*, 1935, **32**, 53; 1936, **33**, 53.

² "Smekal-Raman-Effekt," *Ergänzungsband* 1931—37, Julius Springer, 1938.

³ Gauthier-Villars, Paris, 1936.

⁴ John Wiley and Sons or Chapman and Hall, 1938.

of the Conference on Spectroscopy held at the Massachusetts Institute of Technology in July, 1937.

The Hydrogen Bond and Association.—The existence of some form of a "hydrogen bond" in the structure of certain chemical compounds has been recognised for some years, although the exact nature of such a bond has been, and still is, the subject of much discussion and controversy. Within the past two years it has become clear that infra-red spectroscopy offers an entirely new but very promising approach to this problem. This is not because the hydrogen bond itself gives a characteristic absorption, but because the existence of such a bond alters the position and intensity of characteristic absorption bands due to certain groups in the molecule. For instance, some of the best known examples of a hydrogen bond occur either within (intramolecular) or between (extramolecular) molecules containing a hydroxyl group. Now this group has a fundamental frequency of vibration very close to 3700 cm^{-1} , which is practically unaffected by changes in the rest of the molecule but is extremely sensitive to any alteration in the hydroxyl bond, since the vibration is almost entirely confined to that group. If therefore the hydrogen atom of the hydroxyl group becomes involved in either an intra- or extra-molecular linkage, then one would expect the characteristic hydroxyl absorption to be affected. The first workers to observe such an effect were O. R. Wulf and U. Liddel⁵ and R. Freymann.⁶ The former noticed that the absorption corresponding to the first harmonic of the fundamental hydroxyl vibration was missing in substances such as *o*-nitrophenol and methyl salicylate where there is supposed to be a chelate ring formed by an intramolecular hydrogen bond; the last observed that the intensity of the characteristic hydroxyl band in certain alcohols increased with temperature, whereas in other cases a change in temperature caused a change in the position of maximum absorption. This work was very quickly extended and developed both by the original and by a host of other workers.⁷ It was soon established that, in general, there are two characteristic regions of absorption from

⁵ *J. Amer. Chem. Soc.*, 1935, **57**, 1464; see also G. E. Hilbert, O. R. Wulf, U. Liddel, and S. B. Hendricks, *Nature*, 1935, **135**, 147; *J. Amer. Chem. Soc.*, 1936, **58**, 548, 2247.

⁶ *Compt. rend.*, 1932, **195**, 39; *Ann. Physique*, 1933, **20**, 243.

⁷ J. Errera and P. Mollet, *Nature*, 1936, **138**, 882; *Compt. rend.*, 1937, **204**, 259; J. J. Fox and A. E. Martin, *Proc. Roy. Soc.*, 1937, **A**, **162**, 419; A. Buswell, V. Deitz, and W. Rodebush, *J. Chem. Physics*, 1937, **5**, 501; W. Gordy, *ibid.*, p. 284; *Physical Rev.*, 1936, **50**, 1151; R. M. Badger and S. H. Bauer, *J. Chem. Physics*, 1936, **4**, 711; 1937, **5**, 605, 839; M. M. Davies and G. B. B. M. Sutherland, *ibid.*, 1938, **6**, 755, 767; R. Freymann, *ibid.*, p. 497. The last reference gives a brief résumé of Freymann's and his co-worker's results from 1932 to July 1938.

the fundamental vibration of the hydroxyl group. The first is a narrow symmetrical band with its centre somewhere between $2.73\ \mu$ and $2.86\ \mu$ (according to the molecule under investigation); the second is a very wide unsymmetrical band, stretching roughly from $2.9\ \mu$ to $3.2\ \mu$, in which the position and intensity of maximum absorption vary both with temperature and with concentration. It was observed that for alcohols dissolved in an inert solvent such as carbon tetrachloride an increase of temperature or an increase in dilution always had the effect of strengthening the narrow band and weakening the broad one. The former was accordingly associated with the unperturbed hydroxyl group, and the latter with a molecule in which the hydrogen of this group has been affected through association with other molecules. In other words, the presence of a hydrogen bond is indicated by the appearance of the wide "association band," as it is sometimes called. In the case of the intramolecular bond, the sharp or "monomeric" hydroxyl band is entirely missing and the wide association band is superimposed on the characteristic CH absorption at $3.1\ \mu$. This explains Wulf and Liddel's early result, from which it was at first wrongly concluded that the presence of an intramolecular bond caused the complete disappearance of hydroxyl absorption.

The case of the carboxylic acids is particularly interesting, in that for these we have more information about the strength of the hydrogen bond than in the alcohols or the chelated compounds. Here the hydroxyl absorption shows very similar characteristics to those found in the alcohols, the monomeric band being at $2.83\ \mu$ (as compared with $2.75\ \mu$ in the alcohols), and the association band of the dimer extends from $3.0\ \mu$ to $3.3\ \mu$. The fact that the association band is fully as wide as in the alcohols indicates that the explanation offered by J. Errera,⁸ viz., that the width of the association band is due to different polymers, cannot be the correct one. We shall return to this question of the width of the association band. An additional feature with the carboxylic acids is that absorption bands due to bonds other than the hydroxyl one are found to be affected by association. Thus several workers⁹ showed that the position of the characteristic carbonyl bond absorption at $5.7\ \mu$ was shifted to shorter wave-lengths by raising the temperature of acetic acid either in the vapour or in dilute solution in carbon tetrachloride. More recently,¹⁰ this shift has been proved to be due to the existence of two distinct bands, one characteristic of the

⁸ J. Errera and H. Sack, *Trans. Faraday Soc.*, 1938, **34**, 728.

⁹ R. H. Gillette and F. Daniels, *J. Amer. Chem. Soc.*, 1936, **58**, 1139; E. L. Kinsey and J. W. Ellis, *J. Chem. Physics*, 1937, **5**, 399; W. Gordy, *ibid.*, p. 284.

¹⁰ M. M. Davies and G. B. B. M. Sutherland, see Ref. (7).

carbonyl bond in the monomer, the other characteristic of the same bond in the dimer. The relative intensity of these can be altered in just the same way as the intensities of the monomeric and dimeric hydroxyl bands. There is this important difference, that the monomeric band is not appreciably narrower than the association band. A similar shift but in the opposite direction in the band at $7\ \mu$ has been resolved into two bands presumably due to the C-O single bond in the monomer and in the dimer. This interpretation is not so certain, for the experimental curves are complicated by the presence of other absorptions in the same region. By employing the empirical relations which exist between force constant and internuclear distance, it is estimated that association increases the C=O distance by approximately 0.015 Å. and decreases the C-O distance by about the same amount.

This method of investigation has been made more than qualitative by measuring the intensity of absorption due to the monomeric hydroxyl group (in the photographic region) at various temperatures and assuming it to be proportional to the number of molecules in the monomeric form. In this way Badger and Bauer⁷ were able to confirm reasonably well the value obtained from vapour-density measurements of 16,400 cal. per mole for the heat of association. R. C. Herman and R. Hofstadter¹¹ reached a similar conclusion working on the intensity of the dimeric fundamental OD band in acetic deuteracid. Both these sets of measurements were on the acid in the vapour. More recently Davies and Sutherland,⁷ working with the acid in solution, have obtained a much lower value (6000—10,000 cal. per mole). They conclude, however, that this value is probably spuriously low, for the absorption coefficient in solution seems to vary with temperature.

The conclusions regarding the nature of the hydrogen bond to be drawn from these experiments are still being crystallised, and much more experimental work is required, particularly on the behaviour of the OH deformation frequency. Certain general deductions may already be formulated, of which the first concerns the change in the O-H distance when the hydrogen atom becomes involved in a hydrogen bond. From the comparatively small alteration in the vibration frequency, it is clear that the change in the internuclear distance must also be small: it may be estimated as not greater than 0.1 Å. Thus in the formic acid dimer the O-H distances must be very close to 1.07 and 1.60 Å. if we take the value given by electron diffraction for the O-O distance, *viz.*, 2.67 Å. In the alcohols, where the change in the frequency is less than in the acids, the alteration in the O-H distance must be correspondingly smaller. The

¹¹ *J. Chem. Physics*, 1938, 6, 540.

question as to whether there is a simple relation between the shift in the frequency and the energy of formation of the hydrogen bond has not been satisfactorily settled, although several suggestions have been made.¹² The fact that the changes in frequency and internuclear distance are relatively small when the hydrogen bond is formed indicates that the source of the energy of association is to be sought rather in ordinary classical electrostatic interactions than in quantum-mechanical effects, although the latter must certainly play some part in the acids. The importance of the contribution of electrostatic terms has been shown by the calculations of R. H. Gillette and J. Sherman¹³ and also of E. A. Moelwyn-Hughes.¹⁴ In this connexion, a recent theory proposed by E. Bauer and M. Magat¹⁵ is of particular interest. These authors have been able to give a quantitative account of the large change in the hydroxyl frequency observed for water in going from the vapour to the liquid and the solid state by considering purely classical electrostatic effects. The essential feature of their treatment is that, in calculating the effect of neighbouring molecules on a specified water molecule, the molecules are not regarded as dipoles which interact, but the interaction between individual "effective" charges is computed. In this way the alteration in the hydroxyl frequency is related to the distance between two neighbouring atoms by taking the Bernal-Fowler model as a basis. According to this theory, the O-H distance alters from 0.972 Å. in water vapour to a mean value of 0.985 Å. in liquid water at normal temperatures, and to 0.989 Å. in ice at 0° K. The well known diffuseness of the Raman bands of water is thus explained as being due to the different internuclear distances which exist between the oxygen atoms in the liquid state. The width of the association band in the alcohols receives a similar explanation, the narrowing of the band with rise of temperature being interpreted as due to the transition from "libration" about a fixed position to "free rotation." It is not so easy to see how the width of the association band in the carboxylic acids can be explained on this theory. It should be added that Bauer and Magat can also explain why the change in the deformation frequency of the hydroxyl group is in the opposite direction to the change in the bond frequency in going from the gaseous to the liquid state. In connexion with Bauer and Magat's treatment of the spectrum of liquid water, mention should also be made of a very interesting paper by P. C. Cross, J. Burnham, and P. A. Leighton¹⁶ on the Raman spectrum

¹² R. M. Badger and S. H. Bauer; J. J. Fox and A. E. Martin, *loc. cit.*, Ref. (7).

¹³ *J. Amer. Chem. Soc.*, 1936, **58**, 1135.

¹⁴ *J.*, 1938, 1243.

¹⁵ *J. Phys. Radium*, 1938, **9**, 319

¹⁶ *J. Amer. Chem. Soc.*, 1937, **59**, 1134.

of water at different temperatures up to the critical point. They interpret the changes in the structure of the bands in terms of the perturbed radial frequencies in a broken-down ice structure, but their method has been criticised by Bauer and Magat because certain arbitrary interactions are introduced to get agreement with experiment.

Free Rotation.—The problem of free rotation about a single bond is another subject on which the spectroscopist can now give the physical chemist considerable help. Evidence on this point may be obtained from either infra-red or Raman spectra. In each case it may be detected through its effect on the symmetry of the molecule (and consequently on the selection rules governing the appearance of vibration frequencies in absorption or scattering), but in the absorption case its effect on the rotational structure of the bands may also be detectable.

In ethane the effect of a restricting potential on the appearance of the vibration-rotation spectrum has been very fully investigated by J. B. Howard,¹⁷ who concludes that, although there is no definite evidence for or against free rotation from a purely vibrational analysis, yet the rotational fine structure of certain bands in the infra-red indicates a minimum value of 2000 cal. per mole for the potential restricting rotation. This would appear to be confirmed by the measurements of the heat capacity by G. B. Kistiakowsky, J. R. Lacher, and F. Stitt,¹⁸ although it is not in agreement with the analysis of the vibrational spectrum made by E. Bartholomé and J. Karweil.¹⁹ Another simple molecule for which the existence of a restricting potential has been established from the rotational structure is methyl alcohol. Here, A. Borden and E. F. Barker²⁰ have shown that the rotation of the hydroxyl group about the C-O bond is restricted by a potential barrier of 500 ± 100 cm.⁻¹. In the case of formic acid, S. H. Bauer and R. M. Badger²¹ deduce that the restricting potential is so high that the hydroxyl group may be regarded as clamped firmly in the *cis*-position. This conclusion has since been questioned by I. E. Coop, N. R. Davidson, and L. E. Sutton,²² whose measurements of the dielectric polarisation indicate that free rotation or a transition to the *trans*-position may take place between 40° and 140°. Analysis of the rotational structure of certain bands of methylamine²³ has indicated that here also the rotation is very restricted at ordinary temperatures.

The detection of free rotation by its effect on the Raman spectrum

¹⁷ *J. Chem. Physics*, 1937, **5**, 451.

¹⁸ *Ibid.*, 1938, **6**, 407.

¹⁹ *Z. physikal. Chem.*, 1938, **B**, **39**, 1.

²⁰ *J. Chem. Physics*, 1938, **6**, 553.

²¹ *Ibid.*, 1937, **5**, 852.

²² *Ibid.*, 1938, **6**, 905.

²³ H. W. Thompson and H. A. Skinner, *ibid.*, p. 775.

of the molecule has been considered by S. Mizushima, Y. Morino, and their co-workers²⁴ in a series of papers dealing with the halogenated ethanes, the *o*-halogenophenols, the carboxylic acid monomers, sulphur monochloride, and other substances containing C-C, C-O and S-S bonds. This method does not give reliable results unless supplementary information from infra-red spectra or dipole moments is available.

Rotation in the Solid State.—The idea that certain molecules might be free to rotate about their equilibrium positions in the crystalline lattice was introduced by L. Pauling²⁵ in 1930 in order to account for the entropy of hydrogen and for anomalous peaks occurring in the specific-heat and the polarisation curves at certain (transition) temperatures. There have been several attempts to get direct spectroscopic proof of this phenomenon, but so far without much success. G. Hettner²⁶ has investigated the infra-red absorption spectrum of hydrogen chloride above and below the transition point (98° K.) at which rotation is supposed to set in. Instead of finding signs of rotational structure, he obtained above 98° K. a single maximum, but below this temperature he found a doublet the relative intensities of whose components varied with temperature. A little later, P. Shearin,²⁷ using higher dispersion, claimed to have found individual rotation lines below the transition point in the same substance. This work of Shearin's has not been confirmed in a recent investigation by E. Lee, G. B. B. M. Sutherland, and C. K. Wu,²⁸ who, using dispersion equal to Shearin's, have exactly repeated Hettner's result below the transition point. The latter authors have also investigated deuterium chloride, where they find, not two, but three maxima. Infra-red studies have also been made on hydrogen bromide, hydrogen iodide,²⁹ carbon dioxide,³⁰ and the ammonium salts,³¹ but so far without producing any clear-cut evidence. From Raman spectra the evidence is also rather unsatisfactory in that no actual rotational structure has been detected from a solid. A. C. Menzies and H. R. Mills³² have investigated the Raman spectra of ammonium chloride and bromide above and below the transition points. In the case of the chloride, the appearance of a low lattice frequency below the transition point is accounted for by rotation setting in at that temperature. Such a conclusion requires further substantiation, however, particularly in view of the

²⁴ *Sci. Papers Inst. Phys. Chem. Res. Tokyo*, 1937, **32**, 220. This paper contains references to all the previous work.

²⁵ *Physical Rev.*, 1930, **46**, 430.

²⁷ *Physical Rev.*, 1935, **48**, 299.

²⁹ J. Zunino, *Z. Physik*, 1936, **100**, 335.

³¹ R. Pohlman, *ibid.*, 1932, **79**, 394.

³² *Proc. Roy. Soc.*, 1935, **A**, **148**, 407.

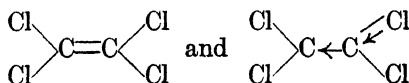
²⁶ *Z. Physik*, 1934, **89**, 234.

²⁸ *Nature*, 1938, **142**, 169.

³⁰ W. Dahlke, *ibid.*, **102**, 360.

fact that later work³³ on the Raman spectrum of ammonium chloride indicates that there are many unexplained peculiarities in this spectrum and that the whole question of the interpretation of such very low Raman frequencies is still very imperfectly understood.

Force Constants and Bond Character.—In the Reports for 1936 methods of obtaining the values of the force constants characterising the resistance offered by a bond to stretching were reviewed, and a small list was given of fairly well accepted values for some of the commoner linkages. The only significant advance to be reported in methods of treatment is a development of the general method of Mannebach in a systematic manner by O. Redlich and H. Tompa.³⁴ When more data are available from isotopic molecules this method is bound to become the only really satisfactory one. Meanwhile, the more approximate methods based on the valency force field continue to yield useful and interesting results. Thus, H. W. Thompson and J. W. Linnett³⁵ have concluded that resonance hybrids probably exist in carbon suboxide and cyanogen, where the variations in the C-C, C-O, and C-N force constants from normal values are real. This last is the crucial point in all approximate methods which suffer from the defect that one can seldom be sure whether variations in the values of a force constant found in going from one molecule to another are real or are due to neglect of interaction terms in the potential function. It is never safe to conclude, because a certain set of force constants will reproduce the observed frequencies, that these are the correct set, since an infinite number of sets exist fulfilling that condition. Unless the isotopic frequencies have been predicted and verified, or the effect of small interaction terms carefully considered, one should accept values of force constants and deductions based on them with considerable caution. For instance, it is possible to correlate the frequencies in the spectrum of tetrachloroethylene with a set of potential constants giving an abnormally low value (6.2×10^5 dynes/cm.) for the C-C force constant. J. Duchesne³⁶ and, later, H. W. Thompson and J. W. Linnett³⁷ have interpreted this as arising from resonating structures thus :



Recently, however, Duchesne³⁸ has shown that a more complete potential function (of the Mannebach type) yields equally good

³³ F. T. Holmes, *J. Chem. Physics*, 1936, **4**, 88. ³⁴ *Ibid.*, 1937, **5**, 529.

³⁵ *J.*, 1937, 1384, 1399.

³⁶ *Nature*, 1937, **139**, 288.

³⁷ *J.*, 1937, 1393.

³⁸ *Nature*, 1938, **142**, 256.

agreement with a value for the C-C force constant which is practically the same as that in ethylene (8.5×10^5 dynes/cm.). Which is the correct interpretation is still uncertain.

The complete potential function for the water molecule has been very thoroughly investigated by G. W. King,³⁹ who shows that the substitution of deuterium for hydrogen does not change the potential function within the accuracy of measurement of the vibrational levels. This enables the value of the angle to be calculated as $107^\circ 22'$, agreeing quite satisfactorily with that obtained from rotational analysis,⁸² viz., 105° . All the potential constants are determined for the complete potential function (allowance being made for cubic and quartic terms). This shows that valency and central force constants are equally important and that the cross terms are not negligible, at least with respect to the lowest frequency. The problem of the most suitable potential function for the ethylene molecule has engaged the attention of several workers,⁴⁰ but is not yet satisfactorily cleared up, as there is still some doubt regarding the assignments of some of the fundamental frequencies. For those frequencies of which the assignment is not in question, the generalised function of C. Mannebach and A. Verleysen⁴⁰ gives the best agreement as tested by prediction of the isotopic frequencies in tetra-deuteroethylene. A modified valency force field suggested by H. W. Thompson and J. W. Linnett,⁴⁰ which seemed to give excellent correlation of the ethylene frequencies, is found to give poor agreement when used to predict the isotopic frequencies.⁴¹ More recently, J. J. Fox and A. E. Martin⁴⁰ have tried modifying Thompson and Linnett's function by the addition of two more cross terms. These authors do not consider the problem as a whole but are more interested in showing that the value for the C-H force constant is intermediate between that found for the same bond in formaldehyde and in acetylene. It had previously been pointed out by Sutherland and Dennison⁴⁰ that the difference in the C-H force constant in methane and in acetylene corresponded to a difference in the C-H distance in those two molecules. Following this, Thompson and Linnett⁴² tried to correlate the different C-H force constants with differences in the C-H distances in different molecules,

³⁹ *J. Chem. Physics*, 1937, **5**, 405, 413.

⁴⁰ G. B. B. M. Sutherland and D. M. Dennison, *Proc. Roy. Soc.*, 1935, **A**, **148**, 250; J. M. Delfosse, *Ann. Soc. sci. Bruxelles*, 1935, **55**, 114; L. G. Bonner, *J. Amer. Chem. Soc.*, 1936, **58**, 34; C. Mannebach and A. Verleysen, *Ann. Soc. sci. Bruxelles*, 1936, **56**, 349; 1937, **57**, 31; Y. Tchang, *ibid.*, 1938, **58**, 87; H. W. Thompson and J. W. Linnett, *J.*, 1937, 1376; J. J. Fox and A. E. Martin, *Proc. Roy. Soc.*, 1938, **A**, **167**, 257.

⁴¹ G. B. B. M. Sutherland and G. K. T. Conn, *Nature*, 1937, **140**, 644.

⁴² *J.*, 1937, 1396.

largely as a test of the empirical relations of Badger and Clark between force constant and internuclear distance (see next section). Although Fox and Martin would seem to have established that the C-H bond in ethylene is intermediate in length between those in acetylene and in formaldehyde, their other conclusion regarding the assignment of one of the ethylene frequencies has since been questioned by G. K. T. Conn and G. B. B. M. Sutherland,⁴³ whose work on the spectrum of tetradeuteroethylene leads them to still another assignment of the ethylene frequencies.

Force Constant and Internuclear Distance.—The empirical relation between force constant and bond length has been further investigated. C. H. Douglas Clark and J. L. Stoves,⁴⁴ working on a very wide range of non-hydride diatomic molecules and "di-atoms," claim to have demonstrated that Clark's relation gives a better fit than either Badger's⁴⁵ or H. S. Allen and A. K. Longair's.⁴⁶ H. W. Thompson and J. W. Linnett⁴² investigated the applicability of Badger's and of Clark's relation to the C-O, C-H, and C-C linkages in various polyatomic molecules, and in so far as reliable values of force constants and distances were available, found that both gave reasonable agreement, Clark's being somewhat superior. In the Report for 1936 only Badger's form of the relation was quoted, viz.,

$$r_e = (c_{ij}/k_e)^{\frac{1}{2}} + d_{ij}$$

where r_e is the equilibrium internuclear distance, k_e is the bond force constant, and c_{ij} and d_{ij} are constants depending on the positions of the constituent atoms in the periodic table. Clark⁴⁷ gives the relation in the form

$$r_e = (k_{gr}/\omega_e n^{\frac{1}{2}})^{\frac{1}{2}}$$

where k_{gr} is a constant depending on the periods in which the two atoms are situated, n is the "group number" (defined as the sum of the number of valency electrons of both atoms), and ω_e the fundamental frequency. It will be noticed that this equation relates, not the force constant, but the vibration frequency to the internuclear distance. Such a formulation is clearly wrong from the dynamical point of view, since it implies that a change of mass (*e.g.*, isotopic) which produces a change in the frequency must therefore produce a change in the interatomic distance. Of course, except for deuterium, the isotope effect is small, but formally the relation is wrong and should be written in the form

$$r_e = (k'_{gr}/k_e n)^{\frac{1}{2}}$$

⁴³ *Proc. Roy. Soc.*, 1939, A., in the press.

⁴⁴ *Phil. Mag.*, 1936, 22, 1137.

⁴⁵ *J. Chem. Physics*, 1935, 3, 710.

⁴⁶ *Phil. Mag.*, 1935, 19, 1032.

⁴⁷ *Ibid.*, 1934, 18, 459.

Because of this fact, H. S. Allen and A. K. Longair ⁴⁶ proposed the formula

$$\omega_e r_e^3 \mu^{\frac{1}{2}} = K$$

where μ is the reduced mass of the di-atom and K is a period constant. All of these relations are obviously approximations to the truth, and which is most successful depends partly on the choice of arbitrary constants to be varied in going from one molecule to another. For instance, Allen and Longair's has only one adjustable constant, whereas each of the others has two. Moreover, Clark varies his value of k_r within a group where Badger keeps c_{ij} constant. The theoretical basis for such relations has been sought by R. A. Newing ⁴⁸ and more recently by G. B. B. M. Sutherland. ⁴⁹ Starting from a general expression for the mutual potential energy of the two atoms of the form

$$V = \beta/r^n - \alpha/r^m \quad . \quad . \quad . \quad . \quad (1)$$

the latter author has shown that relations of the type found by Badger and by Allen and Longair are to be expected, the different relations arising from the particular values chosen for the exponents m and n in (1). For instance, $n = 4$ gives the Allen-Longair relation, whereas $m = 1$ gives the Badger relation. From the same assumption it may also be shown that a relation of the form

$$D = k_e r_e^2 / mn$$

exists between the dissociation energy D and the internuclear distance r_e . Such a relation had been deduced empirically by R. Mecke ⁵⁰ several years earlier. The empirical connexion between force constant, inter-nuclear distance, and heat of rupture of a bond has also been considered in a very suggestive paper by J. J. Fox and A. E. Martin. ^{50a}

Advances in General Theory.—Except in the evaluation of force constants mentioned earlier, progress here is largely concerned with the interaction between vibration and rotation in polyatomic molecules. This is essentially an extension of the work of E. Teller and L. Tisza ⁵¹ and of M. Johnston and D. M. Dennison ⁵² (see *Ann. Reports*, 1935), who considered the perturbations in rotational structure caused by a degenerate vibration which itself gives rise to an internal angular momentum. H. H. Nielsen ⁵³ has considered the very interesting case of formaldehyde, where the vibrations of

⁴⁶ *Phil. Mag.*, 1935, **19**, 759.

⁵⁰ *Leipziger Vorträge*, 1931.

⁵¹ *Z. Physik*, 1932, **73**, 791.

⁵³ *J. Chem. Physics*, 1937, **5**, 818.

⁴⁹ *Proc. Indian Acad. Sci.*, 1938, **8**, 341.

^{50a} *J.*, 1938, 2106.

⁵² *Physical Rev.*, 1935, **48**, 868.

the methylene group as a unit in two planes perpendicular through the C-O axis are so close that they partly overlap, giving a pseudo-doubly degenerate vibration of the type referred to above. The resulting perturbations in the rotational structure have been computed, the general effect being to enhance the intensity and diminish the spacing of the rotational lines on the sides of the bands adjacent to one another. The agreement with the observed spectrum is very satisfactory⁵⁴ and enables those two frequencies to be assigned with certainty, showing that all previous interpretations of the formaldehyde spectrum were wrong. A somewhat similar problem in which the rotational structures of one of the methane bands is perturbed by the close proximity of another fundamental has been satisfactorily cleared up by H. A. Jahn and W. H. J. Childs.⁵⁵ Such phenomena are bound to be of frequent occurrence in the perpendicular bands of molecules possessing three-fold or higher axes of symmetry. Their elucidation is more than a matter of spectroscopic interest since it yields information about the potential constants of the molecule.

An important paper by R. M. Badger and L. R. Zumwalt⁵⁶ has just appeared on the shapes of the envelopes of the absorption bands of asymmetrical rotators. It will be recalled (see *Ann. Reports*, 1935) that this was one of the few outstanding problems in the theory of vibration-rotation spectra. As the great majority of molecules fall into this class and have moments of inertia so great that their rotational fine structure cannot be resolved, a knowledge of the theoretical envelopes and their dependence on the values of the moments of inertia is clearly of the first importance. The general treatment of the effect of non-rigidity on the equations for the asymmetrical rotator including centrifugal distortion has been given by C. Eckart⁵⁷ and also by E. B. Wilson and their co-workers.⁵⁸ Two other papers are worthy of attention in this section. The first deals with a mechanical method of solving the secular determinantal equation arising in the normal vibration problem;⁵⁹ the second is a systematic treatment by H. J. Bernstein⁶⁰ of the symmetrical modes of vibration of a series of typical molecules having two-, three-, and four-fold axes of symmetry.

⁵⁴ E. S. Ebers and H. H. Nielsen, *J. Chem. Physics*, 1937, **5**, 822.

⁵⁵ *Nature*, 1938, **141**, 916; H. A. Jahn, *Proc. Roy. Soc.*, 1938, **A**, 168, 469.

⁵⁶ *J. Chem. Physics*, 1938, **6**, 711.

⁵⁷ *Physical Rev.*, 1935, **47**, 552; A. Weinberg and C. Eckart, *J. Chem. Physics*, 1937, **5**, 517.

⁵⁸ E. B. Wilson and J. B. Howard, *ibid.*, 1936, **4**, 260; E. B. Wilson, *ibid.*, p. 313; 1937, **5**, 617.

⁵⁹ D. P. MacDougall and E. B. Wilson, *ibid.*, p. 940.

⁶⁰ *Ibid.*, 1938, **6**, 718.

Structural Problems.

Linear Molecules.—Part of a band in the spectrum of $^{13}\text{C}^{16}\text{O}_2$ has been observed in atmospheric absorption by A. H. Nielsen,⁶¹ the agreement with the predicted position from A. Adel and D. M. Dennison's potential constants⁶² being perfect. Certain anomalies in the fine structure of the bands of carbon disulphide have been noted by C. R. Bailey.⁶³ The spectrum of diacetylene has been considered by several workers⁶⁴ and on current analyses appears to yield an abnormally low value for the C—C single-bond force constant (2.85×10^5 dynes/cm.) although the C \equiv C and C—H force constants are practically the same as in acetylene. The spectra of carbon suboxide,⁶⁵ cyanogen,⁶⁶ and various acetylene derivatives⁶⁷ have also received considerable attention, and approximate values for the bond force constants derived. The case of methylacetylene is particularly interesting because in this molecule G. Herzberg, F. Patat, and H. Verleger⁶⁸ were able to resolve the rotational fine structure and show that the C—C single-bond distance was 1.462 ± 0.005 Å., which is considerably smaller than the normal value for this distance, viz., 1.50 ± 0.02 Å.

Spherical Molecules.—The absorption spectrum of tetradeutero-methane has been investigated by A. H. Nielsen and H. H. Nielsen.⁶⁹ The agreement with predictions based on Johnston and Dennison's treatment⁵² of methane is not very satisfactory. There are certain anomalies in the rotational structure indicating interaction between vibration and rotation of a higher order than that considered by Johnston and Dennison which probably accounts for the lack of agreement. Additional structure of a similar kind has been found by E. Lee and G. B. B. M. Sutherland⁷⁰ in the spectrum of germane, and had also been found in silane by W. B. Steward and H. H. Nielsen,⁷¹ although the latter may possibly be an isotope effect.

⁶¹ *Physical Rev.*, 1938, **53**, 983.⁶² *Ibid.*, 1933, **43**, 716; **44**, 99.⁶³ *Nature*, 1937, **140**, 851.⁶⁴ B. Timm and R. Mecke, *Z. Physik*, 1935, **94**, 1; T. Wu and Y. Shen, *Chinese J. Physics*, 1936, **2**, 128; G. Glockler and F. T. Wall, *J. Chem. Physics*, 1937, **5**, 813.⁶⁵ H. W. Thompson and J. W. Linnett, *J.*, 1937, 1291; W. Engler and K. W. F. Kohlrausch, *Z. physikal. Chem.*, 1936, *B*, **34**, 214; R. C. Lord and N. Wright, *J. Chem. Physics*, 1937, **5**, 642.⁶⁶ S. C. Woo, *J. Chinese Chem. Soc.*, 1935, **3**, 301; H. W. Thompson and J. W. Linnett, *J.*, 1937, 1399.⁶⁷ G. Glockler and F. T. Wall, *Physical Rev.*, 1937, **51**, 529 [see also Ref. (64)]; R. M. Badger, *J. Chem. Physics*, 1937, **5**, 178.⁶⁸ *J. Physical Chem.*, 1937, **41**, 123.⁶⁹ *Physical Rev.*, 1938, **54**, 118.⁷⁰ *Proc. Camb. Phil. Soc.*, 1939, in the press.⁷¹ *Physical Rev.*, 1935, **47**, 828.

The work of Jahn and Childs on methane has already been noted.⁵⁵ The assignments of the fundamental frequencies and the values of the bond constants in tetramethylmethane and tetramethylsilane have been investigated by F. T. Wall and C. R. Eddy.⁷² The fine structure in the Raman frequencies of carbon tetrachloride has been shown to be entirely accountable as an isotope effect and not due to a lack of symmetry in the carbon valencies, but it has not been sufficiently resolved to enable one to use it as a discriminant between the various types of force field which have been proposed for this molecule.⁷³

Symmetrical-top Molecules.—The spectroscopic data on the methyl halide molecules have been critically re-examined by Sutherland,⁷⁴ who arrives at values for the carbon-halogen distances which are markedly different from those obtained by the diffraction method. New work on the spectra of the pyramidal molecules trideutero-phosphine and arsine by G. B. B. M. Sutherland, Cheng-Kai Wu, and E. Lee⁷⁵ has enabled them to obtain quite accurate values for the dimensions of those molecules. One of the double frequencies of ammonia which has always been difficult to assign has finally been fixed by E. F. Barker⁷⁶ as having its centre at 3407 cm^{-1} and not at 3450 cm^{-1} as given in the 1936 Report. Earlier work on the Raman spectrum of boron trifluoride has been shown to contain spurious lines,⁷⁷ and C. R. Bailey, J. B. Hale, and J. W. Thompson's assignment⁷⁸ of the fundamentals, based on the infra-red spectrum, has been confirmed. A. Borden and E. F. Barker²⁰ have made the first satisfactory study of the infra-red spectrum of methyl alcohol vapour. Their values for the two larger moments of inertia are $35.18 \times 10^{-40}\text{ g.-cm}^2$ and $33.83 \times 10^{-40}\text{ g.-cm}^2$, i.e., the molecule is practically a symmetrical top. If one assumes that the dimensions of the methyl group are the same as in the methyl halides and the O-H distance is equal to that in water, one arrives at a value for the C-O distance of $1.425 \pm 0.005\text{ \AA.}$, which agrees well with the diffraction value⁷⁹ of $1.44 \pm 0.02\text{ \AA.}$ The spectra of methyl and deuteromethyl deuteri alcohols have also been investigated by E. F. Barker and G. Bosschieter,⁸⁰ but the assignment of the fundamental frequencies is not yet quite certain.

⁷² *J. Chem. Physics*, 1938, **6**, 107.

⁷³ C. K. Wu and G. B. B. M. Sutherland, *ibid.*, p. 114.

⁷⁴ *Trans. Faraday Soc.*, 1938, **34**, 325.

⁷⁵ *Trans. Faraday Soc.*, 1939, in publication.

⁷⁶ *Physical Rev.*, 1937, **52**, 250.

⁷⁷ D. M. Yost, D. DeVault, and E. N. Lassettre, *J. Chem. Physics*, 1938, **6**, 424.

⁷⁸ *Proc. Roy. Soc.*, 1937, **A**, **161**, 107; *J. Chem. Physics*, 1937, **5**, 275.

⁷⁹ L. O. Brockway, J. Y. Beach, and L. Pauling *J. Amer. Chem. Soc.*, 1935, **57**, 2693.

⁸⁰ *J. Chem. Physics*, 1938, **6**, 563.

Asymmetrical-top Molecules.—The pure rotation spectrum of water has been reinvestigated and satisfactorily interpreted for the first time by H. M. Randall, D. M. Dennison, N. Ginsburg, and L. R. Weber.⁸¹ The dimensions given by Mecke⁸² are confirmed but the large effects due to centrifugal forces had to be carefully computed before satisfactory agreement could be obtained. The spectrum of hydrogen sulphide has been the subject of some controversy. The values of the moments of inertia given in the former Report (1936) are not in question, but A. D. Sprague and H. H. Nielsen⁸³ have suggested that a value of 85° for the vertical angle is necessary in order to account for the gross structure of certain of the fundamental absorption bands. On the other hand, B. L. Crawford and P. C. Cross⁸⁴ have defended Cross's original choice of 92° on the basis of the intensities of the individual lines in the band at 10,100 μ . Which is the correct value will be uncertain until the structure of the fundamental bands has been interpreted in detail. For the present, the higher value is to be preferred, since it depends on a more detailed analysis of band structure. The correct vibrational analysis of the formaldehyde spectrum would appear to have been given for the first time by E. S. Ebers and H. H. Nielsen.⁸⁵ The frequencies given in the 1936 Report should be replaced by the following set: 2875, 2780, 1750, 1500, 1278 and 1165 cm^{-1} . These frequencies are satisfactorily correlated by a valency force field, an excellent check being provided by the frequencies of the dideuteroformaldehyde molecule which the same authors have observed. From an analysis of the rotational structure of a band of formic acid in the photographic region, S. H. Bauer and R. M. Badger²¹ have evaluated the moments of inertia of this molecule as 85.2, 74.4, and 10.81×10^{-40} g.-cm.². Several important papers on the absorption spectra of monomeric and dimeric forms of both light and heavy formic and acetic acid have also appeared,⁸⁶ but the complete vibrational analyses have still to be accomplished. The absorption spectrum of hydrogen peroxide has been investigated by C. R. Bailey and R. R. Gordon,⁸⁷ who find that their results, coupled with earlier data on the Raman spectrum of this molecule, support the model proposed for it by W. G. Penney and G. B. B. M. Sutherland.⁸⁸ Several papers have appeared on the spectra of light and heavy ethylene,⁸⁹

⁸¹ *Physical Rev.*, 1937, **52**, 160.

⁸² *Ann. Reports*, 1935, **32**, 61.

⁸³ *J. Chem. Physics*, 1937, **5**, 85.

⁸⁴ *Ibid.*, p. 621.

⁸⁵ *Ibid.*, 1938, **6**, 311.

⁸⁶ R. C. Herman and R. Hofstadter, *ibid.*, pp. 531, 534, 540.

⁸⁷ *Trans. Faraday Soc.*, 1938, **34**, 1133.

⁸⁸ *Ibid.*, 1934, **30**, 898; *J. Chem. Physics*, 1934, **2**, 492.

⁸⁹ M. de Hemptinne, J. Jungers, and J. M. Delfosse, *ibid.*, 1938, **6**, 319; also Refs. (40), (41), (43).

but the assignment of a few of the fundamental frequencies is still open to question and much of the theoretical work will have to be repeated in view of premature assumptions regarding those assignments. The spectrum of allene⁹⁰ has also been investigated, and the value obtained for the moment of inertia (97.0×10^{-40} g.-cm.²) shows that the C-C distance must be virtually the same as in ethylene (1.33 Å.). An assignment of the vibration frequencies has also been proposed.⁹¹ The absorption spectrum of carbonyl chloride has been investigated by C. R. Bailey and J. B. Hale, and the fundamental frequencies assigned. The force constants calculated from a valency force field indicate that resonance occurs between different structures.⁹² The infra-red and Raman spectra of certain uranyl salts have been studied by G. K. T. Conn and C. K. Wu,⁹³ who conclude that the uranyl group is probably not linear.

Deuterium Compounds.—A useful collection of the data available on the spectra of deuterium compounds up to the end of 1936 has been prepared by G. Champetier.⁹⁴

G. B. B. M. S.

3. THE ADSORPTION OF GASES ON PLANE METAL SURFACES.

1. *Introduction.*

Some experiments on the interchange of energy between gas atoms and solids in which Knudsen's thermal accommodation coefficient was measured showed that the accommodation coefficient of helium on tungsten is profoundly affected both in magnitude and in the nature of its temperature variation when all adsorbed films are removed from the surface of the metal.¹ The accommodation coefficient with an ordinary metal, when no particular precautions are taken to ensure a bare surface, is about 0.3 at room temperature and this rises to 0.36 at 90° K. With a clean surface, on the other hand, the temperature variation is as shown in Fig. 1. It will be seen that at 79° K. the very low value of 0.025 is obtained. The curve suggests that, as the absolute zero is approached, the accommodation coefficient approaches the value zero, *i.e.*, the collisions of the gas atoms with the solid become more and more nearly perfectly elastic. No doubt, however, at sufficiently low temperatures adsorption of helium would begin and ultimately condensation in

⁹⁰ E. Eyster, *J. Chem. Physics*, 1938, **6**, 580.

⁹¹ J. W. Linnet and W. H. Avery, *ibid.*, p. 686.

⁹² C. R. Bailey and J. B. Hale, *Phil. Mag.*, 1938, **25**, 98.

⁹³ *Trans. Faraday Soc.*, 1938, **34**, 1483.

⁹⁴ "Tables Annuelles de Constants et Données Numeriques," Hermann & Cie., Paris, 1937.

¹ J. K. Roberts, *Proc. Roy. Soc.*, 1932, **A**, **135**, 192.

bulk would take place, so that the lowest portions of the curve would not be realised in practice. The following physical picture explains why the collisions become elastic at low temperatures. Suppose the solid can be regarded as an assembly of Planck oscillators all of identical frequency ν : this assumption was made by Einstein when he first worked out the quantum theory of the temperature variation of the specific heat of solids. When a gas atom interacts with such an assembly, energy transfers can only take place in amounts of $n\hbar\nu$, where n can have the values 0, 1, 2, 3, etc. At temperatures at which the mean thermal energy is smaller than $\hbar\nu$, a considerable number of the atoms of the solid will be in the ground state. When

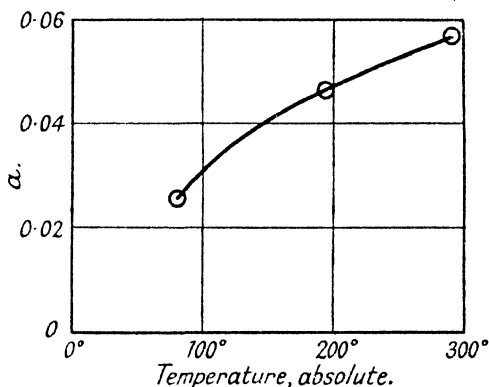


FIG. 1.

Accommodation coefficient, a , of helium with tungsten as a function of temperature.

a gas atom interacts with such an atom, the only possible interchange of energy that can take place is that the gas atom gives up energy to the solid atom, and the smallest amount of energy that the solid atoms can take is $\hbar\nu$. The number of gas atoms that have energy $\hbar\nu$ to give up becomes progressively smaller as the temperature gets lower, and thus the proportion of gas atoms which can undergo a change of energy on interacting with the solid becomes smaller and smaller as the temperature approaches the absolute zero. It is evident that similar considerations will apply when account is taken of the fact that all the oscillations are not of the same frequency. The detailed theory of this effect has been given by A. F. Devonshire,² who has developed the earlier work of Fowler, Jackson, Mott, and others.

With neon, the change in the magnitude of the accommodation coefficient is even greater. At room temperature for an ordinary

² *Proc. Roy. Soc.*, 1937, A, 158, 269. References to the earlier work are given here.

metal when no particular precautions are taken to ensure a bare surface the value is 0.6, and for clean tungsten it is about 0.06. The difference between the temperature variation for helium and for neon is of interest from the point of view of interatomic forces but will not be discussed here. The large change mentioned suggested that the accommodation coefficient of neon would be a sensitive indicator for studying the adsorption on bare tungsten of traces of other gases mixed with the neon.

The first gas chosen for study in this way was hydrogen, and some results obtained are illustrated in Fig. 2 in which the

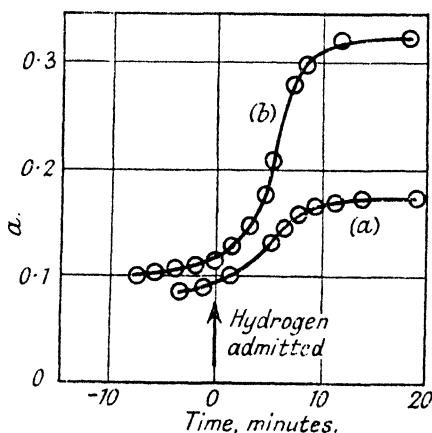


FIG. 2.

*Effect of hydrogen on the accommodation coefficient of neon :
Curve (a), 295° K. ; curve (b), 79° K.*

accommodation coefficient of neon with a clean tungsten surface is plotted as a function of the time in experiments at 295° K. and at 79° K. Even when every precaution is taken to remove adsorbable impurities from the neon, traces remain, and their effect is shown by the small drift at the beginning of the experiment. At the point shown by the arrow, a trace of hydrogen sufficient to produce a pressure of 10^{-4} mm. of mercury was admitted, and the accommodation coefficient of the neon immediately began to rise. The pressure of the neon was about 0.1 mm., so the rise was not due to any direct effect of the hydrogen in transferring heat. We are therefore forced to the conclusion that the hydrogen is adsorbed on the bare tungsten, and that the presence of the adsorbed film alters the accommodation coefficient of neon. Other experiments in which different amounts of hydrogen were admitted showed that, if its partial pressure was 10 times as great, the final value

of the accommodation coefficient was not affected. This suggests saturation, *i.e.*, that the film is complete, at the lower pressure. This was confirmed by experiments by a different method (see p. 56).

This result is in marked contradiction with what had been found in earlier work³ on the adsorption of hydrogen on tungsten, in which the ordinary methods were used and the metal was in the form of a powder. There was no rapid adsorption even at comparatively high pressures, but only a slow take-up of gas and all the phenomena associated with the term activated adsorption, which we shall not discuss. The essential point is that, since no rapid adsorption was observed and since the present experiments have shown that on bare tungsten the complete film is formed rapidly at very low pressures, it must be concluded that in the earlier powder experiments the tungsten was not bare when the hydrogen was admitted, in spite of the fact that these particular experiments with tungsten powder were carried out with great care.

Some general consequences of this result may now be noted. K. F. Bonhoeffer and A. Farkas⁴ have measured the rate of the ortho-para hydrogen conversion on tungsten and other metals at room temperature and have suggested that the mechanism of this conversion is that hydrogen molecules strike the tungsten surface, are adsorbed with dissociation, recombine on the surface, and then re-evaporate in the equilibrium proportion corresponding to the temperature of the metal. This suggestion requires the assumption that re-evaporation of hydrogen from an adsorbed film on tungsten occurs rapidly and continuously at room temperature. The present experiments, and particularly those described below, show that this re-evaporation does not, in fact, occur, and that the film is extremely stable. It is evident that in the experiments of Bonhoeffer and Farkas the tungsten was not bare but was covered with a film of hydrogen, or possibly of oxygen not removed before the experiment began. The conversion must take place above this first layer either by exchange with the atoms in the first layer, if they are hydrogen, or by some interaction between hydrogen molecules in a possible second layer. The details are irrelevant to the present discussion, and in any case are still a matter of speculation, but it is important to point out that the mechanism of Bonhoeffer and Farkas cannot be maintained, although it appears to be widely accepted and applied in other ways. Similar remarks would apply to the exchange reaction between hydrogen and deuterium.

In this connexion it may be mentioned that it has also been

³ W. Frankenburger and A. Hodler, *Trans. Faraday Soc.*, 1932, **28**, 229.

⁴ *Z. physikal. Chem.*, 1931, **B**, **12**, 231. For a general account see A. Farkas, "Orthohydrogen, Parahydrogen and Heavy Hydrogen," pp. 96—101, Camb. Univ. Press (1935).

shown by the two independent methods⁵ that at room temperature and at liquid-air temperature on a bare tungsten surface nitrogen at pressures of the order of 10^{-4} mm. of mercury is rapidly adsorbed to a considerable extent. Some experiments by R. S. Burdon⁶ with another metal, mercury, are of interest too. He has shown that, if a new mercury surface is formed in the presence of hydrogen, a complete film is adsorbed which is stable when the pressure is reduced to 10^{-4} mm. of mercury, but that unless this precaution is taken, i.e., unless the mercury surface is formed in the presence of the hydrogen to ensure that the gas comes into contact with bare metal atoms, no such adsorption is observed.

2. Measurement of Heat of Adsorption on a Filament.

It is of interest to study the properties of films formed under these conditions as widely as possible, and in order to do this a method has been developed for measuring the heat of adsorption on a fine filament, the filament itself being used as a calorimeter.⁷ The principle of the method is the same as that of any method in which heats of adsorption are measured calorimetrically, the only differences being that the amounts of gas involved are very small, so the work must be done at very low pressures and a Pirani gauge must be used for their measurement, and that the amounts of heat involved are small, the temperature rise of the filament being only about 0.01° . To measure this rise, the filament is put in a sensitive Wheatstone bridge so that the change in its resistance when adsorption takes place may be determined. The precautions necessary to produce and maintain a clean surface must, of course, be taken.

The apparent superficial area of the effective part of the filament was 0.55 cm.^2 . If we assume, as is usually done following Langmuir, that the 110 plane is the important one in the surface, the number of tungsten atoms in the surface is $\rho \times 7.8 \times 10^{14}$. If the 100 plane is the important one,⁸ the number of tungsten atoms in the surface is $\rho \times 5.5 \times 10^{14}$, where ρ is a roughness factor which will probably lie between 1 and 2. The total numbers of hydrogen molecules adsorbed in five independent experiments were 4.2, 4.4, 4.3, 3.3 and 3.8×10^{14} . Thus, whichever plane is important, with a reasonable value of ρ we have one atom of hydrogen for each atom of tungsten. The experiments showed that, until the film was

⁵ J. K. Roberts, *Nature*, 1936, **137**, 659; A. B. Van Cleave, *Trans. Faraday Soc.*, 1938, **34**, 1174

⁶ *Proc. Physical Soc.*, 1935, **47**, 460.

⁷ J. K. Roberts, *Proc. Roy. Soc.*, 1935, **A**, **152**, 445.

⁸ R. P. Johnson, *Physical Rev.*, 1938, **54**, 459.

complete, the whole of the hydrogen was taken up by the tungsten, *i.e.*, that the equilibrium pressure was lower than could be detected by the gauge ($< \text{about } 10^{-7} \text{ mm.}$).

The variation of heat of adsorption with amount adsorbed in four experiments is shown in Fig. 3. The results for any given experiment are plotted with the same symbol, and the relative values for different amounts adsorbed in any particular experiment could be determined much more accurately than the absolute values, which are used in comparing different experiments. It will be seen that the relation between heat of adsorption and amount adsorbed is approximately linear. K. F. Herzfeld⁹ pointed out that forces

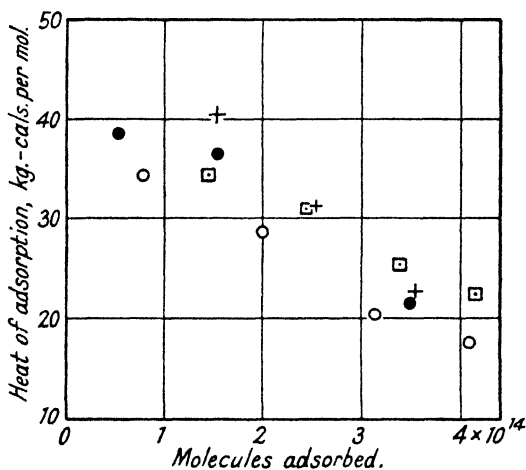


FIG. 3.

Variation of heat of adsorption of hydrogen on tungsten with amount adsorbed.

between adsorbed particles can give rise to variation in the heat of adsorption as the surface becomes covered, and in order to discuss these results it is necessary to have a theory of adsorption which takes these forces into account.

3. *Mobile and Immobile Adsorbed Films.*

In considering the interpretation of these results in terms of the forces between adsorbed particles it is necessary to distinguish carefully between mobile and immobile films and to discuss these two general types separately from the theoretical point of view. By a mobile film we mean one in which the energy of activation necessary to enable a particle to move from the site on which it is adsorbed to a neighbouring unoccupied site is small compared

⁹ *J. Amer. Chem. Soc.*, 1929, **51**, 2608.

with kT . In such a film, particles will move freely from site to site, and at any instant the distribution of particles on the surface under the influence of their mutual forces will be an equilibrium Boltzmann distribution.

If, on the other hand, the energy of activation necessary to enable a particle to move from the site on which it is adsorbed is $\gg kT$, the particles will not move freely over the surface but will remain fixed on the sites on which they are first adsorbed. In an immobile film of this type the distribution of particles on the surface at any instant will not necessarily be an equilibrium Boltzmann distribution. It should be mentioned that an equilibrium distribution can be set up on the surface by the processes of evaporation and condensation themselves, but, if the energy of activation for migration is greater than kT , much more will the heat of evaporation be greater than kT and the probability that a particle will evaporate will be even smaller than that it will migrate. During the occurrence of any process with an immobile film we shall assume that the particles remain fixed where they are first adsorbed.

The theoretical problem is to determine for any type of film the average distribution of particles on the surface for any given total number of adsorbed particles. The exact solution of this problem, taking into account the fact that the energy of a single adsorbed atom in its lowest state is a continuously varying function of its position on the surface, would be extremely complicated. A general indication of the behaviour that would be expected can be obtained by simplifying the problem along the lines first followed by Langmuir in his treatment of the case when there is no interaction. It is well known that he made a great advance when he suggested that, owing to the lattice structure of the solid, there would be a strong localisation of adsorption forces at definite places on the surface, particularly if these forces were chemical in origin. The effect of this can be represented by assuming that there is a definite number, say n_s , of sites per unit area available for adsorption. We retain this assumption and assume further ¹⁰ that, when two particles are adsorbed on neighbouring sites, there is an interaction energy V between them, but, if they are on more distant sites, the interaction energy is negligible;* V is positive if the potential energy arises from repulsive forces. We suppose throughout that the probability

¹⁰ See R. Peierls, *Proc. Camb. Phil. Soc.*, 1936, **32**, 471, who develops a theory first given by Fowler when discussing attractive forces in connexion with critical condensation conditions. A similar treatment can be applied, as here, to repulsive forces.

* For a discussion of this assumption, see J. K. Roberts, "Some Problems in Adsorption," Section 2-7, Cambridge Physical Tracts, Camb. Univ. Press, in course of publication,

that a molecule condenses, when it strikes a vacant site, is independent of the state of occupation of neighbouring sites.

Let us consider an immobile film in which each molecule in the gas phase occupies one site on the surface. There is no appreciable re-evaporation. It is evident that at each stage in the adsorption process the number of occupied neighbouring sites around any site will on the average be θz , where z is the number of neighbours to a given site and θ is the fraction of the total number of sites which are occupied. Thus the heat of adsorption per molecule will be

$$q_0 - z\theta V,$$

where q_0 is the heat of adsorption on a bare surface; *i.e.*, the heat will be a linear function of θ .

For a mobile film, on the other hand, the particles will always tend to arrange themselves in the configuration of lowest energy,

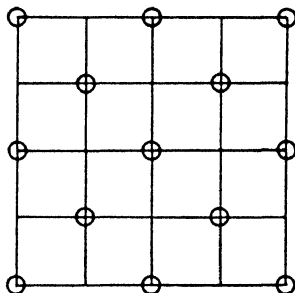


FIG. 4.

State of lowest energy for a quadratic lattice at $\theta = 0.5$ when there is a repulsive force between particles on neighbouring sites.

and the thermal motion will resist this tendency and give actual configurations in accord with Boltzmann's law. Consider a surface in which each site for adsorption has four neighbouring sites as in Fig. 4, in which the sites for adsorption are at the intersections of the lines. The adsorbed molecules are represented by circles. It will be seen that up to $\theta = 0.5$ the particles can arrange themselves as shown in the figure, so that the interaction energy is zero. Hence, up to $\theta = 0.5$ for this model, in the state of lowest energy the heat of adsorption will remain constant at q_0 . It will then drop sharply to $q_0 - 4V$ as illustrated by the curve marked *a* in Fig. 5. If the fact that the particles are distributed according to Boltzmann's law is taken into account, detailed calculations show that the effect is to round the corners of this curve¹¹ to a greater or less extent according to the value of V/kT . This is shown in the figure for various values of $\eta = e^{-V/kT}$.

¹¹ J. S. Wang, *Proc. Roy. Soc.*, 1937, **A**, 161, 127.

At the other extreme we can consider a model in which the potential energy is uniform all over the surface so that there is two-dimensional lateral free motion in the adsorbed film.¹² For values of θ not greater than 0.5 there will be a general similarity between the shape of the curve representing the variation of heat of adsorption with θ and those in Fig. 5. In general, for all mobile films with repulsive forces there will be a tendency for the heat of adsorption to vary slowly with θ at the beginning of the formation of the film.

Similar considerations apply to adsorption with dissociation,¹¹ and for the sake of definiteness we shall assume, as is generally done, that, when hydrogen is chemisorbed on a metal, dissociation

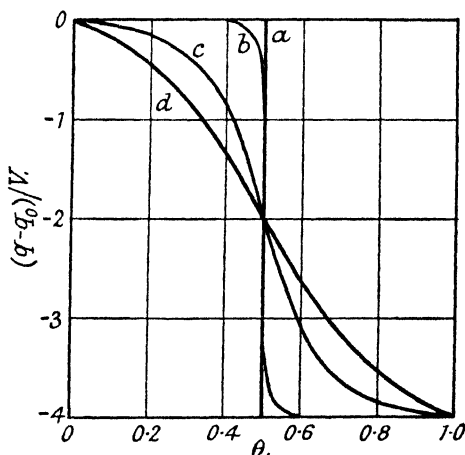


FIG. 5.

Variation of heat of adsorption with fraction of surface covered for a quadratic lattice. Curve a, $\eta = 0$; curve b, $\eta = 5.5 \times 10^{-4}$; curve c, $\eta = 0.082$; curve d, $\eta = 0.368$. $\eta = e^{-V/kT}$.

occurs.¹³ It is not necessary to discuss adsorption with dissociation in detail here as the aim is to give a general account of the physical results. The essential point is that the experimental behaviour is in accord with what would be expected for an immobile film and not with what would be expected for a mobile film with the high interaction energy necessary to account for the large change in heat of adsorption as the surface becomes covered. A further point is that it can be shown that, for a film formed with dissociation, the kinetics of formation is different for a mobile and for an immobile

¹² F. J. Wilkins, *ibid.*, 1938, A, 164, 496.

¹³ For a discussion of this assumption see J. K. Roberts, *op. cit.* The general considerations brought forward would apply, apart from changes in detail, to any other type of adsorption in which each adsorbed molecule occupies more than one site.

film.¹⁴ In order to investigate the condensation of hydrogen on tungsten at room temperature, R. C. L. Bosworth¹⁵ has used a modification of I. Langmuir and K. H. Kingdon's method¹⁶ for measuring contact potentials, improved by A. L. Reimann¹⁷ and developed by Bosworth and E. K. Rideal¹⁸ to study some properties of sodium films on tungsten. He has shown that the kinetic behaviour is in accord with what would be expected for an immobile film, but not for a mobile one (for a fuller discussion of this, see Roberts¹³).

4. Holes and Gaps in Immobile Adsorbed Films.

It has been pointed out by the Reporter⁷ that, unless each gas molecule occupies one site and one site only on the surface, *immobile* films will necessarily have gaps in them; *i.e.*, when adsorption has finished taking place, there will still be vacant sites left on the surface on which no further adsorption can occur; in other words, the molecules will not be packed as tightly on the surface as is possible. These vacant sites will probably be important centres of catalytic activity.¹⁹ The reason for the occurrence of these vacant sites or holes in the adsorbed film can be understood by considering as an example adsorption of diatomic molecules with dissociation. We suppose that the two atoms into which the molecule dissociates occupy two neighbouring sites on the surface and that, if a molecule from the gas strikes a place on the surface where two neighbouring sites are vacant, the probability of its condensing is independent of the state of occupation of neighbouring sites. It is evident that, as the film is built up, certain single vacant sites will be found to be completely surrounded by occupied sites. Such sites will be able to play no part in the adsorption process and will remain bare. By using a model of the surface²⁰ and occupying it by choosing pairs of sites at random by drawing cards, it was found that 8% of the total number of sites remained bare. The proportion of bare sites will, of course, depend on the type of adsorption.²¹

Suppose that there is oxygen present in the gas phase. These uncovered tungsten atoms will undoubtedly exert a greater

¹⁴ J. K. Roberts, *Proc. Roy. Soc.*, 1937, A, 161, 141.

¹⁵ *Proc. Camb. Phil. Soc.*, 1937, 33, 394.

¹⁶ *Physical Rev.*, 1929, 34, 129.

¹⁷ *Phil. Mag.*, 1935, 20, 594.

¹⁸ *Proc. Roy. Soc.*, 1937, A, 162, 1.

¹⁹ J. K. Roberts, *Nature*, 1935, 135, 1037.

²⁰ For a general discussion of the use of models to obtain the properties of immobile films, see J. K. Roberts, *Proc. Camb. Phil. Soc.*, 1938, 34, 399.

²¹ See, *e.g.*, *idem, ibid.*, p. 577, where a different type of adsorption is considered in which there is no dissociation but each particle occupies more than one site.

attraction on impinging oxygen molecules than the other parts of the surface, and it seems possible that oxygen molecules will be found adsorbed on these holes. In measuring the heat of adsorption of oxygen on tungsten, the Reporter ⁷ found some oxygen adsorbed with a heat of adsorption in the neighbourhood of 50,000 cal. per mol., as contrasted with a heat of over 100,000 cal. per mol. on bare tungsten, and suggested that this adsorption of a comparatively small quantity with a lower heat was due to adsorption of molecular oxygen on these holes.

In order to see if he could obtain any further experimental evidence consistent with the existence of these holes, A. B. Van Cleave ²² carried out some experiments on the adsorption of oxygen, using the accommodation coefficient of neon as a detector. The Reporter ⁷

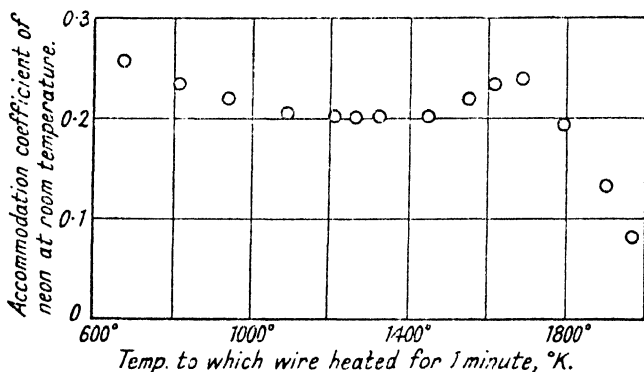


FIG. 6.

Effect of heating a tungsten filament covered with oxygen to various temperatures.

had already used this method and, in agreement with the result obtained in measuring the heat of adsorption, had shown that some oxygen in addition to that in the well-known stable film is adsorbed. In the first place, it is important to mention that, by admitting larger amounts of oxygen than had been used by the Reporter, Van Cleave showed that changes in the accommodation coefficient could be obtained so large that they could not be accounted for by adsorption in the holes alone. It was therefore necessary to suppose that, in addition to adsorption in the well-known stable film and in the holes in this film, adsorption could take place in a second layer on top of the stable film. The essential part of Van Cleave's experiment from the present point of view is the following. After the oxygen had been deposited on the tungsten, the filament was heated by a current i for one minute to various temperatures plotted as abscissæ in Fig. 6. The wire was then allowed to cool, and the

²² *Trans. Faraday Soc.*, 1938, **34**, 1174.

accommodation coefficient α of neon at room temperature was measured. Since there was always a residual trace of oxygen in the neon in this experiment, the value of α showed a drift with time, and in Fig. 6 the value extrapolated to the instant at which the current i was cut off is plotted as ordinate in each experiment. It will be seen that heating the wire to 1100° or 1200° K. for one minute reduced the accommodation coefficient to 0.20. This value presumably corresponds to the presence of the well-known stable film, and the higher values which persisted when the wire was only heated to 1100° K. or lower are due to the presence of a second less stable one. Removal of the first or stable film began at about 1750° K. Heating the wire to temperatures between about 1500° and 1700° K. caused an *increase* in the value of the accommodation coefficient. This effect occurred consistently, and was presumably due to some rearrangement in the film, a possible interpretation being that the first film becomes mobile at these temperatures, thus allowing the gaps to move about and so to come together and be filled up from the residual traces of oxygen in the gas phase. Van Cleave's results are therefore consistent with, although they cannot be taken as definitely establishing, the view that the stable film contains holes or gaps.

5. *The Production of Atomic Hydrogen by Hot Tungsten.*

Among processes involving the adsorption of hydrogen on tungsten one of the most interesting is the production of atomic hydrogen by the hot metal, and it has recently been possible to give a satisfactory account of this process. This is probably the simplest chemical surface reaction that is known, and because of this it is possible to consider in some detail the various mechanisms by which the reaction can proceed. We shall see that it is difficult to distinguish between these mechanisms. This makes one realise very strongly that, in more complicated surface reactions involving a number of gases where numerous combinations of mechanisms could be proposed, the fact that a given mechanism accounts for the observed kinetics does not necessarily mean that the mechanism is correct.

The first experiments on this subject were carried out by I. Langmuir.²³ When a tungsten filament is heated to a sufficiently high temperature in hydrogen contained in a glass vessel, the walls of which are cooled in liquid air, he showed that there is a continuous diminution of pressure, and interpreted this as being due to the production by the hot tungsten of atomic hydrogen which is adsorbed on the surface of the glass.

²³ *J. Amer. Chem. Soc.*, 1912, **34**, 1310; 1915, **37**, 417; see also *Gen. Electric Rev.*, 1926, **29**, 153.

To obtain quantitative data in this connexion, it is obviously essential to use an efficient method of trapping the hydrogen atoms, since, if it can be assumed that every atom produced is trapped before it recombines with another atom, the rate of disappearance of gas, which is obtained from the volume of the vessel and the rate of diminution of pressure, gives a measure of the rate of production of atoms. Langmuir's measurements themselves showed that glass cooled in liquid air is not consistently efficient in this way, since the rate of production of atoms under definite conditions appeared from them to be very variable. Atomic hydrogen is known to react with molybdenum oxide. G. Bryce²⁴ therefore carried out some experiments in which, in order to trap the atoms, this oxide was deposited to a depth of more than 50 layers on the walls of the tube containing the hydrogen. Subsidiary experiments indicated the efficiency and lack of fatigue effects in the oxide as a trapping agent. Bryce showed that the earlier estimates of the rates at various temperatures of the tungsten were too low by factors which were all greater than 200. He showed, too, that the rate varies rapidly with the temperature of the tungsten, and determined the law of this variation. Uncertainties due to inefficient trapping in the earlier experiments had obscured this effect.

After correcting for the effect of temperature distribution in the filament, Bryce showed that the number n of atoms produced per cm.² per second is given by

$$n = 2.5 \times 10^{24} \sqrt{p} e^{-45,000/RT}$$

where p is the pressure of the hydrogen in mm. of mercury, the temperature of the gas being 0°; T is the absolute temperature of the tungsten, and R is in calorie units. This formula applies over a temperature range of 1148—1420° K. and a pressure range of 2.4— 37×10^{-3} mm. of mercury. It will be seen that, over this range of conditions at a given filament temperature, the rate of production is proportional to the square root of the hydrogen pressure.

To account for these results theoretically, we must consider the processes occurring at the surface of tungsten in the presence of hydrogen. The equilibrium condition in the gas phase for the reaction $H_2 = 2H$ is

$$p_1 = 10^3 \sqrt{K} \sqrt{p_2} \quad . \quad . \quad . \quad . \quad (1)$$

where p_1 and p_2 are the partial pressures (in dynes per cm.²) of atomic and molecular hydrogen and K is the equilibrium constant with pressures measured in atmospheres. Consider a tungsten box maintained at the required temperature and containing hydrogen,

²⁴ *Proc. Camb. Phil. Soc.*, 1936, **32**, 648.

the surface of the tungsten being quite free from oxygen and other adsorbed impurities. The processes occurring at the surface must themselves be able to set up and maintain the degree of dissociation of the hydrogen corresponding to the temperature of the walls and the pressure quite apart from any reactions taking place in the gas phase. Three pairs of surface reactions must be considered and, according to the principle of detailed balancing, each pair must balance individually. These are :

- (i) (a) Evaporation of atoms from the adsorbed film. (b) Atom from gas hits bare surface and is adsorbed.
- (ii) (a) Two neighbouring adsorbed atoms combine and evaporate as a molecule. (b) Molecule strikes the surface where two neighbouring sites are bare and is adsorbed as atoms.
- (iii) (a) Gas atom strikes adsorbed atom, combines with it, and the two evaporate as a molecule. (b) Gas molecule strikes bare surface, one atom is adsorbed, and the other goes into the gas phase.

If we neglect the effect of interactions between adsorbed atoms and write down the condition for the balance of these processes, it can be shown²⁵ by using equation (1) that each pair leads to the condition

$$\theta/(1 - \theta) = A\sqrt{p_2} \quad . \quad . \quad . \quad (2)$$

where A , which is constant at constant temperature, can be represented in three different ways given by

$$A = \frac{10^3\sqrt{K}}{\mu_1} \cdot \frac{\alpha}{v} = \frac{1}{\sqrt{\mu_2}} \left(\frac{\beta}{\eta} \right)^{\frac{1}{2}} = \frac{(m_1/m_2)^{\frac{1}{2}}}{10^3\sqrt{K}} \cdot \frac{\delta}{\gamma} \quad . \quad . \quad (3)$$

In these equations $\mu_1 = \sqrt{(2\pi m_1 kT)}$, $\mu_2 = \sqrt{(2\pi m_2 kT)}$, v is the number of atoms evaporating per second per unit area from a complete film, α is the probability that a gas atom striking a bare surface is adsorbed, η is the number of molecules evaporating per second per unit area from a complete film due to the recombination of adsorbed atoms, and β the probability that a molecule striking a bare surface is adsorbed; γ is the probability that a gas atom striking an adsorbed atom combines with it and the two evaporate as a molecule, and δ the probability that a molecule striking a bare surface breaks up so that one atom is adsorbed and the other escapes into the gas phase. Equation (2) is the isotherm for this type of adsorption.

It will be seen that, of the processes enumerated above, (i) (a) and (iii) (b) both give rise to the presence of atoms in the gas phase. We shall now show²⁶ that the \sqrt{p} law is obtained, if, under the con-

²⁵ J. K. Roberts, *Proc. Camb. Phil. Soc.*, 1936, **32**, 154.

²⁶ J. K. Roberts and G. Bryce, *ibid.*, p. 653.

ditions of the experiments, (i) (α) is the important process and the surface is very sparsely covered, *i.e.*, θ is small. It is obtained equally if (iii) (b) is the important process and the surface is nearly completely covered, *i.e.*, θ is nearly unity. Further, we shall show that the temperature variation in the rate of production is the same for the two processes. Thus, it is not possible with the results available to distinguish between them from kinetic considerations alone, and it is not easy to extend the range of the experimental conditions widely.

When θ is small, equation (2) becomes $\theta = A\sqrt{p_2}$. The rate of evaporation of atoms from the film is $v\theta$, and, with the first value of A given in (3), this rate is

$$v\theta = 10^3(\alpha/\mu_1)\sqrt{K}\sqrt{p_2} \quad . \quad . \quad . \quad . \quad . \quad (4)$$

At constant temperature this is proportional to $\sqrt{p_2}$. Equation (2) actually gives the fraction of surface covered when the gas is at the same temperature T° as the wire. Since, at the filament temperatures with which we are concerned, the degree of dissociation is small, it can be taken as giving to a first approximation the fraction of surface covered when the wire is at T° and the gas at 0° . To this approximation we can treat μ_1 and the condensation coefficient α as constants. The variation with temperature of the rate of production of atoms is then due entirely to the variation with temperature of \sqrt{K} .

Now consider process (iii) (b). When θ is nearly unity, equation (2) becomes $1/(1 - \theta) = A\sqrt{p_2}$. The rate of production of atoms is $\delta p_2(1 - \theta)/\mu_2$ or, from the last equation, $\delta\sqrt{p_2}/A\mu_2$. The last value of A from (3) being used, this becomes $10^3(\gamma/\mu_1)\sqrt{K}\sqrt{p_2}$. This, as we have said, is also at constant temperature proportional to $\sqrt{p_2}$. If we regard γ as independent of T , we have again that the temperature variation in the rate of atom production is due entirely to the temperature variation of \sqrt{K} . The values of K have been calculated from the data given by W. F. Giaque,²⁷ but using the value 101,000 cal. for the heat of dissociation from spectroscopic data instead of the older value 102,800 used by him. These values of K being used, the relative rates of production of atomic hydrogen at the tungsten surface at various temperatures can be obtained immediately if the above view is correct. Thus, if the rate at one temperature (the highest) is taken as known, the rates at other temperatures can be calculated. The results of these calculations and also the measured rates are given in the accompanying table. When account is taken of the approximations in the calculation, the agreement between calculated and observed values is very satisfactory.

²⁷ *J. Amer. Chem. Soc.*, 1930, **52**, 4816.

The Reporter¹⁴ has shown that, when the interaction between adsorbed particles is taken into account, the above considerations

Temp., °K.	Production of H atoms per cm. ² per sec. $\times 10^{-14}$ at $p = 1.25 \times 10^{-2}$ mm. of mercury.	
	Obs.	Calc.
1420	316	(316)
1338	115	103
1243	32	22
1148	7	4

are not affected, and has discussed this whole question more fully elsewhere.¹³

In order to decide whether process (i) (a) or process (iii) (b) is the important one, it is necessary to determine whether, under the conditions obtaining in Bryce's experiments, the surface is sparsely or nearly fully covered with hydrogen. Bosworth¹⁵ has investigated this problem, using the contact-potential method, and has concluded that the surface is nearly fully covered. Thus we must suppose that the production of atomic hydrogen in the range of conditions considered is predominantly due to the process in which a molecule hits a bare place on the surface and one atom is adsorbed and the other passes into the gas phase.

In addition, some important qualitative observations on the effect of oxygen poisoning on the rate of production of atomic hydrogen have been made by G. Bryce,²⁸ who has shown that some of the inferences drawn by earlier workers in this field will have to be modified. For example, the removal of poisoning oxygen in the presence of hydrogen, which was attributed by Langmuir to a flank attack of the hydrogen on the adsorbed oxygen, is shown to take place in an exactly similar way when hydrogen is absent.

6. *The Removal and Formation of Adsorbed Films on Tungsten.*

I. Langmuir and D. S. Villars²⁹ first measured the heat of evaporation of oxygen from tungsten by measuring the temperature variation of the evaporation rate. Similar measurements have recently been carried out by M. C. Johnson and F. A. Vick³⁰ by measuring the time variation of the thermionic emission from a filament with an oxygen film on it. In order to carry out these measurements, they developed a method using a suitable oscillograph to follow the rapid changes involved, and Johnson and A. F. Henson³¹ have used the method to study the deposition of oxygen films at very high

²⁸ *Trans. Faraday Soc.*, 1937, **33**, 782.

²⁹ *J. Amer. Chem. Soc.*, 1931, **53**, 486.

³⁰ *Proc. Roy. Soc.*, 1935, **A**, **151**, 296.

³¹ *Ibid.*, 1938, **A**, **165**, 148.

temperatures. Their results suggest the possibility that the oxygen film thus formed is of a different nature from that formed at ordinary temperatures.¹³ Bosworth and Rideal³² have also given a preliminary account of a determination of the heat of evaporation of oxygen, using the same method and detecting the film by measuring the contact potential. The Reporter²⁰ has discussed the general theory of the method.

When oxygen is admitted to tungsten already covered with hydrogen, the Reporter,⁷ using the heat of adsorption method described in Section 2, has shown that the oxygen is adsorbed and that each molecule which goes on to the surface throws off a molecule of hydrogen.

7. *The Theory of Adsorption.*

An important advance in the fundamental theory of adsorption was made by R. H. Fowler³³ when he showed that the Langmuir adsorption isotherm can be deduced from statistical considerations without postulating any particular mechanisms for condensation and evaporation. He³⁴ later extended the statistical theory to include the effects of attractive interactions between adsorbed particles, and showed that with sufficiently large attractive forces critical phenomena would occur, and at temperatures below the critical temperature there would, at a given stage in the adsorption process, be a rapid increase in the equilibrium amount adsorbed with increase of pressure. This same problem was later treated by R. Peierls,³⁵ using the method which Bethe first developed for studying order and disorder problems in alloys. Fowler and Peierls both considered the formation of one layer only of adsorbed atoms, and the extension of the theory to two layers has been carried out by G. P. Dube.³⁶

J. S. Wang¹¹ used the method of Peierls in discussing the effect of repulsive forces between adsorbed particles, and later³⁷ obtained an approximate theory to cover the effect of dipole interactions. Other applications of the method have already been discussed. Mention should be made of papers by G. S. Rushbrooke,³⁸ T. S. Chang,³⁹ and by E. A. Guggenheim⁴⁰ in which some of the assumptions underlying the theory are discussed.

The mechanisms of evaporation and condensation have been discussed in a number of papers by J. E. Lennard-Jones and his

³² *Physica*, 1937, **4**, 925; 1938, **5**, 170.

³³ *Proc. Camb. Phil. Soc.*, 1935, **31**, 260.

³⁴ *Ibid.*, 1936, **32**, 144.

³⁶ *Ibid.*, 1938, **34**, 587.

³⁸ *Ibid.*, p. 424.

⁴⁰ *Proc. Roy. Soc.*, 1938, **A**, **169**, 134.

³⁵ *Ibid.*, p. 471.

³⁷ *Ibid.*, pp. 238, 412.

³⁹ *Ibid.*, p. 224.

collaborators.⁴¹ One of the most interesting results is that even at low temperatures evaporation in two stages is relatively frequent, *i.e.*, the particle is first excited from the ground state to a higher vibrational level and then receives a further quantum of energy from the solid which causes it to evaporate.

J. K. R.

4. CHEMICAL KINETICS.

Just as physical chemistry in these reports has been divided into a number of well-established divisions, so chemical kinetics has been similarly classified. The method is convenient, for the progress made each year may be clearly summarised and assessed; but the consequence is that some branches of the subject are left out or are only cursorily examined. In this Report, therefore, many of the customary topics, such as photochemistry, unimolecular reactions, oxidations and explosions, reactions in solution, have been purposely omitted in order to make way for a discussion of a variety of processes connected in one way or another with the solid state. Such reactions include heterogeneous catalysis, diffusion in solids, thermal decomposition of solids, photo-processes in solids, etc. It must be admitted that the progress made in these lines of research is less striking and often less clear cut than in gaseous or liquid kinetics, but there is no doubt, in spite of greater experimental difficulties, that material advances are being made which put the subject on a more satisfactory footing and justify a discussion of it. First, attention is devoted to the mechanism of heterogeneous catalysis. Here, deuterium has been of great value in discriminating between reaction mechanisms. The original novelty of the discovery of deuterium reactions has disappeared and has been replaced by a more thorough attack in which all possible methods have been employed in close collaboration. Connected with heterogeneous catalysis is the mechanism of diffusion of gases through metals. Here a beginning has been made in isolating and measuring the rate of the interface reaction and the velocity of diffusion through the metal itself. There is, however, still lacking a theory which will correlate velocity of diffusion with the associated energy of activation. An essentially similar process occurs in the interdiffusion of solids where qualitative criteria are now beginning to emerge. Somewhat more complicated is the thermal decomposition of solids, for example, of detonating substances and the dehydration of salt hydrates, although some degree of order is now apparent in this

⁴¹ J. E. Lennard-Jones and A. F. Devonshire, *Proc. Roy. Soc.*, 1936, **A**, **156**, 6, 29; C. Strachan, *ibid.*, 1937, **A**, **158**, 591; J. E. Lennard-Jones and E. T. Goodwin, *ibid.*, 1937, **A**, **163**, 101.

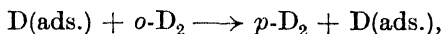
field. Not less complicated are photo-reactions in solids, but fortunately it has been possible to choose simple systems—alkali halide lattices—with which to experiment. The result has been to give fundamental significance to the nature of the absorption spectra and to gain an insight into the primary and secondary photo-processes. Moreover, evidence is not lacking that that knowledge can be applied to the more familiar reactions, such as the photo-decomposition of silver halides or the fluorescence and phosphorescence of sulphides, in order to bring reason into the wide variety of observational data collected over a long period of years.

Heterogeneous Gas Reactions.—Although there have been recent reports on various phases of heterogeneous catalysis, it would appear to be opportune to survey the subject with especial reference to recent developments. As is well known, the basic theory was put forward many years ago by I. Langmuir and illustrated by a series of experiments in comparatively simple systems. Somewhat later, C. N. Hinshelwood further extended the enquiry by adding a number of systems falling into well defined types. Briefly, what the theory¹ did was to attempt, from the observed pressure and temperature dependence of the reaction, to give a picture of the nature and concentration of the adsorbed entities and their precise mode of interaction. Since these early developments, a long list of reactions on as many different catalysts has been investigated without resulting in any material advance in the theory of such processes. In some reactions, for example, it is not possible to correlate the observed pressure dependence with temperature dependence according to the Langmuir theory. This does not, of course, reflect on the theory for, even had the systems been suitable for the application of the theory, and some were not, there are certain problems which had eluded experimental investigation. A case in point may be quoted. At a nickel surface hydrogen will hydrogenate ethane to methane. By the older method, the kinetics may be determined and the mechanism worked out as far as the method will allow. But it is not possible to say whether the ethane is dissociated to two methyl radicals or to an ethyl radical and a hydrogen atom, or whether the hydrogen is dissociated into atoms which in turn attack adsorbed ethane, nor for that matter is it possible to define the rate-determining step in the reaction. The newer technique, utilising para-hydrogen, deuterium, and deuterides, has advanced the problem another whole stage, but the complete solution is not by any means in sight. What deuterium has done is to provide answers to specific questions which had hitherto been only matters

¹ See, e.g., "Kinetics of Chemical Change in Gaseous Systems," 3rd edn., Oxford, Chap. 8.

for uncertain and often wild speculation. It is convenient to consider this section according to the under-mentioned subdivisions.

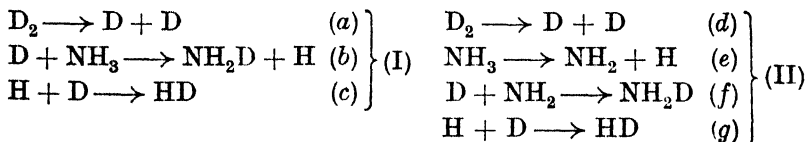
Exchange of deuterium with saturated hydrides. H. S. Taylor and J. C. Jungers² demonstrated qualitatively that deuterium exchanged with ammonia on a synthetic-ammonia catalyst (iron, potassium, and aluminium oxides) at temperatures lower than those at which ammonia is readily formed, the evidence being the change in the ultra-violet absorption spectrum of the ammonia. By employing ortho-deuterium and carrying out a systematic investigation of the kinetics on an evaporated iron catalyst, A. Farkas³ was able to gain a definite idea of the mechanism. The advantage in using ortho-deuterium is that a measurement may be made of its rate of conversion alongside of that of exchange reaction, so that the rate of dissociation of deuterium may be obtained. Two objections might be raised in this connexion. The first is that the ortho-deuterium conversion might be due to the paramagnetism of the catalyst, and the second that the mechanism of the conversion is



i.e., an exchange reaction with the deuterium already adsorbed on the surface of the catalyst. With a number of catalysts it has been shown that the reaction $\text{H}_2 + \text{D}_2 \longrightarrow 2\text{HD}$ goes at about the same speed as the ortho-deuterium conversion; this disposes of the first objection but not directly of the second, and therein lies a possible weakness of the method.

At temperatures in the neighbourhood of 200° , exchange between deuterium and ammonia is much slower than that of the ortho-deuterium conversion, in spite of the fact that the velocity of the latter reaction is strongly inhibited by the presence of ammonia. That ammonia is strongly adsorbed is shown, not only by the fact that the exchange reaction is of zero order with respect to ammonia pressure, but also because inhibition by ammonia becomes irreversible if ammonia is allowed access to the catalyst at 20° , when a small amount of hydrogen can be detected.

As in all reactions of this nature, there are essentially two mechanisms by means of which exchange may occur, *viz.*,



(All the molecules are supposed to be adsorbed on the catalyst.)

² *J. Amer. Chem. Soc.*, 1935, **57**, 660.

³ *Trans. Faraday Soc.*, 1936, **32**, 416.

Since the velocity of conversion is greater than that of exchange (*e.g.*, 100 : 1 at 155°), reactions (a), (c), (d), and (g) are not rate-determining. On account of the slight decomposition of ammonia on admission to a fresh catalyst, Farkas concluded that mechanism (II) is the correct scheme. These conclusions are supported in part by the observation that the apparent energy of activation for exchange, 15 kg.-cals., is somewhat greater than that for conversion, 8 kg.-cals.

In a similar manner, deuterium exchanges with water on typical hydrogenation catalysts which exhibit activated adsorption of hydrogen.⁴ In fact, the water content of such catalysts may be estimated by determining the equilibrium point for the exchange. Likewise, a platinum wire catalyst is effective for this reaction.⁵ Again the para-ortho interconversion is more rapid than exchange, and in addition, the former reaction is inhibited by the water vapour. There is also some degree of reversible poisoning by water vapour. These observations parallel those with ammonia, and therefore the question arises: Does exchange occur between adsorbed atomic deuterium and adsorbed water or fragments of the water molecule such as hydroxyl radicals? The indirect evidence from irreversible poisoning of the catalyst for the para-conversion would indicate that the latter alternative is correct. A variety of organic molecules, *e.g.*, ethyl ether, benzene, acetone, ethyl alcohol, *n*-butanol and 2-ethylhexanol, exhibit exchange in presence of a platinum catalyst.⁶ Naturally, all hydrogen atoms are not equally reactive. For example, those in the alcoholic hydroxy-group exchange more rapidly than those attached to a carbon atom. Roughly, two types of behaviour may be distinguished: (i) reactions in which the para-conversion is much faster than exchange, and (ii) those in which these changes occur at about the same speed. Such a classification is, of course, dependent both on the temperature of the catalyst and on the pressure of the molecule undergoing exchange. Ethyl ether, benzene, and acetone belong to the first class, but ethyl alcohol may be brought into this class if its pressure is reduced from a few mm. to 0.01 mm. in presence of 20 mm. of deuterium. If it is assumed that the hydride is dissociated, then, when the conversion is faster than exchange, the velocity of the latter process is governed by the rate of dissociation of the hydride. On the other hand, when the para-conversion goes at the same speed as the exchange, then the rate of dissociation of deuterium is the rate-determining step, for

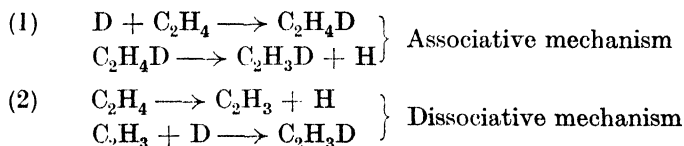
⁴ H. S. Taylor and H. Diamond, *J. Amer. Chem. Soc.*, 1934, **56**, 1821; 1935, **57**, 1256.

⁵ A. Farkas, *Trans. Faraday Soc.*, 1936, **32**, 922.

⁶ A. Farkas and L. Farkas, *ibid.*, 1937, **33**, 378.

in this circumstance the strong adsorption of the hydride limits the area upon which the deuterium molecule may dissociate. The exchange is thus controlled by the replacement of these hydrogen atoms with deuterium. In the same paper a scheme is worked out to account for this behaviour and its relation to exchange occurring at the liquid catalyst interface.

Exchange with unsaturated molecules. With such compounds there is the additional complication of hydrogenation to be taken into account, and the question arises whether the exchange is intimately bound up with the hydrogenation or whether the two processes are independent of each other. With ethylene on nickel, hydrogenation occurs to the exclusion of exchange at low temperatures (20°), while the reverse happens at higher temperatures (200°).⁷ Ethane does not undergo exchange under these conditions, and moreover, at low temperatures the para-hydrogen conversion is inhibited strongly by the ethylene except when the ethylene pressure is low. Somewhat similar behaviour⁸ is obtained with a platinum catalyst, the para-conversion possessing practically the same apparent energy of activation as the hydrogenation reaction. The ratio of conversion rate to hydrogenation rate depends on the relative pressures. Above 150°, there is an inversion of the temperature coefficient of the hydrogenation, similar to that observed for nickel,⁹ the para-conversion then proceeding relatively much faster. In so far as exchange is concerned, two mechanisms are again possible, *viz.*,



From the similarity in apparent energies of activation for para-conversion and hydrogenation, A. and L. Farkas suggest that the latter involves dissociation of the hydrogen when addition to ethylene immediately occurs if an ethylene molecule is in the neighbourhood. The exchange reaction, on the other hand, has a much higher energy of activation. This is attributed to the occurrence of reaction (2), the equilibrium being displaced towards the right, thus decreasing the concentration of adsorbed ethylene molecules. This cuts down the velocity of the hydrogenation reaction and is the cause of the inversion of the temperature coefficient.

⁷ A. Farkas, L. Farkas, and E. K. Rideal, *Proc. Roy. Soc.*, 1934, A, **146**, 630.

⁸ A. Farkas and L. Farkas, *J. Amer. Chem. Soc.*, 1938, **60**, 22.

⁹ E. K. Rideal, *J.*, 1922, **121**, 309; H. zur Strassen, *Z. physikal. Chem.*, 1934, A, **169**, 81.

Exchange of deuterium with liquid benzene, first demonstrated by I. Horiuti, G. Ogden, and M. Polanyi,¹⁰ is also catalysed by nickel and platinum. Under different conditions—platinum in the gas phase—hydrogenation proceeds at a comparable speed,¹¹ the interesting observation being made that the para-conversion is not now inhibited by benzene. Again, it would appear that hydrogenation and exchange have essentially different mechanisms, for the rate of the former is proportional to the first power of the hydrogen pressure and independent of the benzene pressure, whereas the exchange rate is independent of the hydrogen pressure and proportional to the 0.4 power of the benzene pressure. It is suggested that the dissociative mechanism holds good for exchange, but that benzene is only adsorbed on certain selected portions of the surface in which the geometrical arrangement of the platinum lattice is most favourable. Adsorption is complete on those regions.

Exchange reactions between hydrides and deuterides. It will be realised from the foregoing discussion that the para-hydrogen conversion and the rate of formation of HD molecules from H₂ and D₂ provide important information about adsorbed hydrogen, but such observations do not allow any absolutely definite conclusions to be drawn about the nature of the interaction of the hydride with the catalytic surface. To find whether or not a hydride is dissociated on such a surface, the interaction of the hydride with the corresponding deuteride must be investigated. For those molecules which yield absorption spectra in the quartz ultra-violet, a qualitative analysis will serve to demonstrate the appearance of intermediate deuterides. Owing to the complexity of such spectra, infra-red spectra possess many advantages, although the technique is more laborious. W. S. Benedict, K. Morikawa, R. B. Barnes, and H. S. Taylor¹² have described the details of the analytical technique for the methanes and ethanes, which absorb strongly in two regions, *e.g.*, at 2000—3200 cm.⁻¹ owing to valency vibrations, and at 900—1300 cm.⁻¹ owing to deformation vibrations. It has proved possible to estimate the mole-fraction of any individual intermediate deuteride, and thus to say whether a hydride mixture is in a state of equilibrium.

Employing a nickel catalyst, K. Morikawa, W. S. Benedict, and H. S. Taylor¹³ showed that methane and tetradeuteromethane gave the equilibrium amounts of the intermediate methanes when

¹⁰ *Trans. Faraday Soc.*, 1934, **30**, 663; cf. also I. Horiuti and M. Polanyi, *ibid.*, p. 1164.

¹¹ A. Farkas and L. Farkas, *ibid.*, 1937, **33**, 827.

¹² *J. Chem. Physics*, 1937, **5**, 1.

¹³ *J. Amer. Chem. Soc.*, 1936, **58**, 1445.

put into contact with the catalyst. Moreover, the velocity and apparent energy of activation for the exchange reaction $D_2 + CH_4 \longrightarrow CH_3D + HD$ were about the same as those for the interaction of hydride and deuteride. Also it is very probable that under the conditions—high temperature, 200° , active bulk catalysts—the para-conversion would have been very fast. Hence it is established straight away that, not only is methane dissociated into methyl and atomic hydrogen, but that this reaction is the rate-determining step in the exchange reaction. If the deuterium is replaced by its oxide, the velocity of the exchange is much decreased owing to displacement of adsorbed methane by the oxide. With ethane, hydrogenation to methane occurs in addition to exchange. The infra-red technique, supplemented by appropriate chemical analysis,¹⁴ showed again that the exchange rate is governed by the dissociation of the hydrocarbon to ethylene and atomic hydrogen. On the other hand, hydrogenation to methane, which involves splitting of the molecule into two methyl groups, occurs much less readily. The reactions of propane have been analysed in a similar manner, the reactivity of the molecule being somewhat greater than that of ethane. In this way the order in which the various bonds in a hydrocarbon are broken on a nickel catalyst may be determined. The order is as follows, the reactivity increasing down the series : $(CH_4 \longrightarrow CH_3 + H) > (C_2H_6 \longrightarrow 2CH_3) > (C_3H_8 \longrightarrow C_2H_5 + CH_3) > (C_2H_6 \longrightarrow C_2H_5 + H) > (C_3H_8 \longrightarrow C_3H_7 + H) > (H_2 \longrightarrow 2H)$.

Mention has already been made of the difficulty in deciding between the mechanisms for exchange and hydrogenation of unsaturated compounds. It is evident that exchange between hydrides and deuterides will decide the issue for exchange of hydride with deuterium. Experiments¹⁵ with ethylene have shown that no exchange between hydride and deuteride occurs under conditions where the exchange reaction with deuterium is very fast. The associative mechanism for exchange must therefore operate with ethylene. Whether it occurs with other unsaturated molecules is yet to be seen. For ethylene, at any rate, the results mean that both hydrogenation and exchange are similar, in that if another hydrogen atom combines with the associative complex before the latter dissociates ethane will be formed. The problem then is to reconcile the dissimilar kinetics of the two reactions with the essential similarity in mechanism. Such a correlation is indeed difficult and emphasises the remarks made at the beginning of this report; but there is, of course, the possibility that in hydrogenation

¹⁴ K. Morikawa, W. S. Benedict, and H. S. Taylor, *J. Amer. Chem. Soc.*, 1936, **58**, 1795.

¹⁵ G. H. Twigg and G. K. T. Conn, private communication.

the addition of two hydrogen atoms, even from the same molecule, may occur consecutively but so rapidly that the half-hydrogenated state does not exist, under some conditions, long enough to have the opportunity to dissociate.

Relative Velocities of Reactions of Hydrogen and Deuterium.—This question may be considered in two stages. First, measurements of the relative velocities of a number of such reactions have been made to determine to what extent zero-point energy controls the rate of heterogeneous reactions. Secondly, the experience so gained may be applied to discriminate between reaction mechanisms when other methods fail. It is probably true to say that the second stage has not yet been reached although much work has had this object in view.

In surface reactions hydrogen may react more quickly than deuterium by a factor of $\sqrt{2}$, owing to the greater speed of the hydrogen molecule or atom either in getting to the surface or in migrating along it. Besides this factor there is another effect to be taken into consideration. If the reaction involves the activation of a hydrogen bond, then, in virtue of the fact that the zero-point energy of a hydride is at most 41% greater than that of a deuteride, the energy of activation required for the deuteride may be larger, since zero-point energy is known to contribute to the activation energy of reactions.¹⁶ Some time ago H. Eyring and A. Sherman¹⁷ estimated that the difference in zero-point energy of surface hydrides and deuterides of metals commonly used as catalysts was not greater than about 700 cal. At 300° K., the maximum possible ratio of rates will be $\exp(700/RT) = 3$, while at 600° K. the ratio is only 1.7. The reactions which have been studied are the ortho-para conversion of hydrogen and deuterium, on nickel¹⁸ and platinum,¹⁹ the reduction of nitrous oxide and oxygen,²⁰ and of ethane to methane on nickel,²¹ the reduction of copper oxide,²² the reduction of light and heavy ethylene by hydrogen and by deuterium on nickel and on copper.²³ In nearly every reaction the hydrogen reacts more quickly than the deuterium, and sometimes the ratio of rates is greater than can be accounted for by the simple mass factor of

¹⁶ For a summary, see H. W. Melville, *Science Progress*, 1937, **31**, 499.

¹⁷ *J. Chem. Physics*, 1933, **1**, 348.

¹⁸ E. Fajans, *Z. physikal. Chem.*, 1935, **B**, **28**, 247.

¹⁹ A. Farkas and L. Farkas, *J. Amer. Chem. Soc.*, 1938, **60**, 22.

²⁰ H. W. Melville, *J.*, 1934, 797.

²¹ K. Morikawa, W. S. Benedict, and H. S. Taylor, ref. (14).

²² H. W. Melville and E. K. Rideal, *Proc. Roy. Soc.*, 1935, **A**, **153**, 82.

²³ T. Tsucholski and E. K. Rideal, *J.*, 1935, 1701; G. Boris, J. C. Jungers, and H. S. Taylor, *J. Amer. Chem. Soc.*, 1938, **60**, 1982; G. G. Jones and J. C. Jungers, *ibid.*, p. 1999; R. N. Pease and A. Wheeler, *ibid.*, 1935, **57**, 1149.

$\sqrt{2}$. Experimentally, however, it is extremely difficult to measure the difference in the energies of activation for hydrogen and deuterium, since the experimental error in the individual determinations is often of the same order of magnitude as the difference. The same state of affairs exists for the decomposition of ammonia and deuterioammonia²⁴ and of phosphine and trideutero-phosphine²⁵ on tungsten, the ratio of rates giving, without correction for a mass factor, a difference of a few hundred calories. A fair general summary of the present position of this section of kinetics would be that, in a number of heterogeneous processes involving both hydrogen and deuterium, hydrogen reacts faster because of the greater zero-point energy possessed by the hydrogen bond, but the full effect of this factor is annulled to a large extent by the existence of zero-point energy in the transition state. In those reactions where such a difference is observed it may be concluded that the rate-determining step does involve the activation of the hydrogen bond. Further than this it would probably be unsafe to go, and therefore the method will in general be insufficiently accurate to be of any use in settling reaction mechanism. The so-called tunnel effect originally looked for by E. Cremer and M. Polanyi²⁶ does not appear to play any significant part in the above-mentioned reactions.

Activated Adsorption.—By studying the relative rates of adsorption of hydrogen and deuterium on those solids exhibiting the phenomenon, it was also hoped to gain some further information about this process. Measurements have been made on nickel,²⁷ on copper,²⁸ on chromic oxide, and $\text{ZnO} \cdot \text{Cr}_2\text{O}_3$.²⁹ Sometimes hydrogen is more quickly adsorbed than deuterium; the reverse happens under different conditions on the same adsorbent. The phenomena appear to be so complicated that in this particular instance the interpretation of the experiments with deuterium certainly has not clarified the problem.

Diffusion of Gases through Metals.—Although this type of interaction of gases with solids was quantitatively studied more than 30 years ago and sporadically since that time, there has been a revival of interest within the past two or three years. This is due to developments in technique permitting measurements over a

²⁴ J. C. Jungers and H. S. Taylor, *J. Amer. Chem. Soc.*, 1938, **60**, 679.

²⁵ R. M. Barrer, *Trans. Faraday Soc.*, 1936, **32**, 490.

²⁶ *Z. physikal. Chem.*, 1932, **B**, **19**, 443.

²⁷ J. Pace and H. S. Taylor, *J. Chem. Physics*, 1934, **2**, 578; R. Klar, *Naturwiss.*, 1934, **22**, 822.

²⁸ H. W. Melville and E. K. Rideal, *Proc. Roy. Soc.*, 1935, **A**, **153**, 85; R. A. Beebe, E. L. Wildner, and S. Goldwasser, *J. Amer. Chem. Soc.*, 1935, **57**, 2527.

²⁹ J. Pace and H. S. Taylor, ref. (27).

wider range of conditions, and also to the fact that the reactions of the hydrogen modifications and of deuterium have supplied new data which must be incorporated in any theory of diffusion. It was established by O. W. Richardson, J. Nicol, and T. Parnell³⁰ that the diffusion coefficient (D) of hydrogen through platinum is given by $D = \text{const. } p^{1/2} e^{-E_D/RT} \cdot \sqrt{Td}^{-1}$, where p is the pressure on one side of the platinum, the other side of the metal being in a vacuum, E_D is a characteristic constant, and d the thickness of the metal. Later experiments with other metals fully supported the validity of the equation.³¹

Before enquiring further into the significance of the factors in the above equation, the first question which arises is whether diffusion of the gas occurs along the intercrystalline cracks or through the lattice itself. Since the rate of diffusion is sometimes subject to the treatment and condition of the metallic surface, it would appear that intercrystalline cracks are important in this connection. With iron, however, C. J. Smithells and C. E. Ransley³² have shown that diffusion must take place through the lattice, since the rate is not markedly altered by substituting a polycrystalline tube for a tube consisting of a single crystal. It is not impossible that this may prove to be a general phenomenon for hydrogen-metal systems. The appearance of the \sqrt{p} term in the diffusion equation has always been taken to imply that hydrogen atoms migrate through the lattice. There is, however, no doubt that the molecule as such loses its identity in the process, for if para-hydrogen or a mixture of hydrogen or deuterium is used the corresponding equilibrium mixture issues from the other side of the metal.³³ At low pressures, on the other hand, the rate varies with the pressure according to a power higher than $\frac{1}{2}$ ³⁴ (the pressure at which the deviation occurs is higher the lower the temperature). None the less surprising is the fact that the square-root law holds up to at least 112 atmospheres.³⁴ In view of the fact that the rate of diffusion is inversely proportional to the thickness, the general picture of the diffusion process is that a concentration gradient is set up inside the metal, the magnitude of the gradient being proportional to the square root of the hydrogen pressure. Such a mechanism implies that the rate-determining step is not the transfer

³⁰ *Phil. Mag.*, 1904, **8**, 1.

³¹ For a summary, see C. J. Smithells, "Gases and Metals," Chap. 2, Chapman and Hall, London.

³² *Proc. Roy. Soc.*, 1935, **A**, **150**, 172.

³³ A. J. Gould, W. Bleakney, and H. S. Taylor, *J. Chem. Physics*, 1934, **2**, 366.

³⁴ C. J. Smithells and C. E. Ransley, *Proc. Roy. Soc.*, 1935, **A**, **150**, 172; 1936, **A**, **157**, 1936.

of hydrogen molecules to atoms just inside the metal surface, i.e., the interface reaction, but the transport of the atoms within the lattice. Hence, in order to explain the low-pressure dependence of rate upon pressure, Smithells and Ransley suggested that hydrogen molecules adsorbed on the surface controlled the concentration of atoms just inside. The concentration of molecules is supposed to be given by the simple form of the Langmuir isotherm. At high enough pressures this concentration is independent of pressure, and hence the \sqrt{p} law is obeyed; at low pressures the concentration of molecules is proportional to p and thus the rate of diffusion to $p^{3/2}$. At very high pressures, on this hypothesis, there ought to be a limit to the concentration of dissolved hydrogen atoms, whereupon the diffusion rate should become independent of pressure. J. S. Wang³⁵ has put forward a mechanism which evades this difficulty and also accounts for the high and low pressure rates. Besides the two processes envisaged above, i.e., (a) gas molecules strike the surface of the metal and are dissociated, and (b) the passage of adsorbed atoms just inside the metal, an additional process is added, viz., (c) a molecule strikes a vacant place on the surface of the metal, one atom is adsorbed, and the other penetrates inside the metal.

It is evident from these results that the phenomena at the gas-metal interface merited further study. Again, the rates of diffusion of deuterium have been compared with those of hydrogen for the metals copper, nickel, and palladium^{22, 36} in the hope that further light might be brought to bear on the problem. As in heterogeneous reactions, the diffusion rate for hydrogen is somewhat higher than that for deuterium, but the same difficulty arises here as was encountered in interpreting the results for heterogeneous reactions, viz., that the difference in overall energy of activation cannot be accurately determined without making certain assumptions, which are not easy to verify. However, it would appear that the difference is of the order of a few hundred calories.

Experiments with palladium deserve special mention because, not only may the relative rates of diffusion be measured at comparatively low temperatures, but also the relative solubilities under the same conditions.^{22, 37} The heats of solution of hydrogen and of deuterium are calculated from the variation of solubility with temperature. The apparent energy of activation for diffusion,

³⁵ *Proc. Camb. Phil. Soc.*, 1936, **32**, 657.

³⁶ A. Farkas and L. Farkas, *Proc. Roy. Soc.*, 1934, **A**, **144**, 477; W. Jost and A. Widmann, *Z. physikal. Chem.*, 1935, **B**, **29**, 247; A. Farkas, *Trans. Faraday Soc.*, 1936, **32**, 1667.

³⁷ A. Sieverts, *Z. physikal. Chem.*, 1935, **174**, 359.

E_D , is thus corrected by subtracting half the heat of solution to give the true energy of activation for diffusion. It turns out that hydrogen is more soluble than deuterium, the heat of solution being greater by a few hundred calories, presumably owing to a zero-point energy effect, thus producing a greater concentration gradient in the metal and thereby causing the hydrogen to diffuse more rapidly. On correcting for solubility, however, it is found that part of the difference in diffusion rate is actually due to the difference of a few hundred calories in the true energy of activation for diffusion.

By measuring the velocity of the para-hydrogen conversion simultaneously with diffusion, A. Farkas³⁶ determined the velocity of the transformation of molecular into atomic hydrogen at the gas-metal interface. With some specimens of palladium the latter process was far faster than the diffusion rate, and hence the rate of diffusion was not governed by the boundary process. This means that the velocity of the boundary process was sufficient to maintain the concentration of atoms just inside the metal at an equilibrium value very nearly equal to that obtaining if there had been no diffusion through the metal. Conditions were also found where the rates of conversion and diffusion were of the same order of magnitude, indicating that in some circumstances the boundary process may become the rate-determining step.

Finally, mention may be made of the "constant" in the diffusion equation. In spite of big variations in the value of the apparent energy of activation for diffusion, the constant is of a similar order of magnitude for a number of metals, as was pointed out by Smithells and Ransley. It is probable that, if allowance had been made for variation of solubility with temperature, a closer concordance would have been obtained. The theoretical significance is not yet known.

Diffusion in Solids.—The first demonstration of the interdiffusion of two solids was made many years ago in the system gold-lead by Roberts-Austen. Later, the self-diffusion coefficient of lead was measured by J. Gróh and G. von Hevesy,³⁸ using as radioactive indicators thorium-*B* and radium-*D*, and found to be very much smaller than that of gold in lead. At 165°, for example, the respective diffusion coefficients are 1.2×10^{-14} and 5.8×10^{-8} cm.² sec.⁻¹. In order to explain this observation, Hevesy³⁹ suggested that the high mobility of gold is due to the attractive forces between its atoms being smaller than those between lead atoms. Hence a qualitative criterion for diffusion would be that the more akin a

³⁸ *Ann. Physik*, 1920, **63**, 85.

³⁹ G. von Hevesy and W. Seith, *Z. Elektrochem.*, 1931, **37**, 528; G. von Hevesy, *ibid.*, 1933, **39**, 491.

metal is to lead, the smaller should be its diffusion coefficient. W. Seith⁴⁰ confirmed this idea when he found the diffusion coefficients decreased in the order silver, cadmium, mercury, bismuth, thallium, tin. For example, at 250°, the coefficients for the systems Pb-Au, Pb-Sn, and Pb-Pb are respectively 3.5×10^{-7} , 1.5×10^{-11} , 5.1×10^{-11} cm.² sec.⁻¹. One condition that the diffusion should occur in a homogeneous system is that the two components should form a solid solution. Gold just comes within this restriction. A less soluble metal might diffuse more quickly, but with the complication of the formation of a two-phase system. The production of radio-active gold has made possible the measurement of the diffusion coefficient of gold.⁴¹ At 917° it has the value 10^{-9} cm.² sec.⁻¹, and on extrapolation to 165°, 6×10^{-25} compared with 1.2×10^{-14} cm.² sec.⁻¹ for lead.

Reactions in Solids.—The question of reactivity in solids is much more complicated than that of heterogeneous catalysis or even of diffusion in solids, mainly because of the immobility of the atoms and molecules constituting the interface and hence of the fact that interaction only occurs between nearest neighbours in a lattice. The simplest type of reaction is the polymorphic transformation, but this is more properly dealt with by the X-ray crystallographer, for information about the nature of reaction is best obtained by X-ray technique. Of more purely chemical interest, however, are the decomposition of detonating substances and the dehydration of salt hydrates, both of which have received very wide attention from the kinetic point of view, with the result that the data can be co-ordinated to form a homogeneous whole.

Detonating substances may first of all be considered. These solids include molecules such as the alkali and alkaline-earth azides, lead azide, nitrogen tri-iodide, lead styphnate, mercury fulminate, Hg(ONC)₂, etc. The general behaviour exhibited by these substances is that on gentle heating they decompose after the lapse of an induction period, the rate at first increasing and then finally decreasing with time. At higher temperatures, detonation may occur after the expiry of an induction period. If the product of the reaction is a solid, the decomposition will occur at the solid-solid interface and presumably also start from such an interface. It is well known that many solid reactions do not take place if the crystals are as nearly as possible perfect. Imperfections or impurities in a crystal are, however, conducive to reaction and are probably normally present in the crystals of the detonating substance. The induction period is thus due to the time required for these

⁴⁰ Z. *Elektrochem.*, 1933, **39**, 33; 1935, **41**, 872.

⁴¹ H. A. C. McKay, *Trans. Faraday Soc.*, 1938, **33**, 845.

imperfections or nuclei to grow to an effective size. Such sources of imperfection can be produced artificially by α -particles,⁴² fast electrons, X-rays, hydrogen, mercury and argon ions,⁴³ and ultra-violet light,⁴⁴ and the induction period is then reduced or eliminated. The exact nature of the primary process is not yet known in any one case. Once the detonation wave is started, it travels with the maximum possible speed, for it traverses a layer of atoms in a crystal in about 10^{-13} sec., i.e., in a period comparable with a lattice vibration. There is therefore no time lag in the transmission of energy from one layer to the next in a crystal. The question arises, as in all reactions of this nature—in gases, liquid, or solids—whether the energy is specifically transmitted to adjacent molecules or whether it is spread over a wider volume, thereby raising the temperature of a small locality of atoms as a whole. This is a very difficult point to settle, and in fact the discrimination may only be artificial. It might be anticipated, however, that if the latter mechanism is important, a sufficient increase in the number of centres would not only remove the induction period but also increase the velocity of the ensuing reaction. Actually, there is no significant increase in reaction velocity. Energy considerations also throw an interesting light on the mechanism of detonation, as has been shown by W. E. Garner.⁴⁵ The activation energy for the decomposition of lead azide is 38 kg.-cals. This energy, together with the exothermic heat of reaction, if transmitted without loss, would only activate three or four molecules of azide and would consequently not start a spherical detonation wave in which molecules must be activated. The simultaneous decomposition of *two* molecules within the requisite time interval would suffice for the propagation of the detonation wave. Even below the detonation temperature, such a coincidence may easily occur within the course of the induction period, since at 290° 10^{16} molecules per cm^2 or 30 layers of molecules decompose per second. The probability that two adjacent molecules will decompose within 10^{-13} sec. is 4×10^{-9} ; i.e., simultaneous reaction would occur 4×10^4 times per sec./ cm^2 . On the same basis, ternary events may be completely excluded.

So-called nitrogen tri-iodide, $\text{NI}_3 \cdot \text{NH}_3$, may be put in a class by itself, for at pressures below 2×10^{-2} mm. even at 0° detonation occurs immediately.⁴⁶ In presence of ammonia, but not of iodine,

⁴² W. E. Garner and C. H. Moon, *J.*, 1933, 1398.

⁴³ H. Kallman and W. Schrankler, *Naturwiss.*, 1933, **21**, 379.

⁴⁴ Cited by W. E. Garner, *Trans. Faraday Soc.*, 1938, **33**, 908.

⁴⁵ *J.*, 1934, 720; *Trans. Faraday Soc.*, 1938, **33**, 985.

⁴⁶ W. E. Garner and W. E. Latchem, *Trans. Faraday Soc.*, 1936, **32**, 567; F. R. Meldrum, *ibid.*, 1938, **34**, 947.

stable decomposition may be observed. It is suggested that NI_3 molecules either are or furnish the nuclei for initiation of detonation. Ammonia represses the formation of NI_3 , and so no detonation wave can be started.

In dealing with the slow decomposition of detonating substances, general features may be mentioned in that there is an induction period preceding reaction which initially increases exponentially with time. W. E. Garner and D. J. B. Marke⁴⁷ sought to eliminate the troublesome interface by working with sodium and potassium azides under conditions in which the resultant alkali metal was immediately removed. Unfortunately, it is only in presence of the saturated vapour of the metal, and therefore of an interface, that the decomposition rates became reproducible. These reactions may then be compared with those of the alkaline-earth azides, lead azide, and lead styphnate. From the following summarising table it will

Substance.	NaN_3 .	KN_3 .	BaN_3 .	CaN_3 .
Range of temp. for decompn.	240—275°	222—255°	100—130°	60—130°
Energy of activation, kg.-cals.	34.4	35.1	21	18—19
Substance.	SrN_3 .	$\alpha\text{-PbN}_3$.	$\beta\text{-PbN}_3$.	$\text{Pb}[\text{C}_6\text{H}(\text{NO}_2)_3\text{O}_2]$.
Range of temp. for decompn.	100—130°	222—260°	200—270°	225—255°
Energy of activation, kg.-cals.	18	38	(37)	(40)

be observed that the lower the temperature at which decomposition occurs the lower is the energy of activation. This regularity does not apply to some molecules, such as mercury fulminate, trotyl,⁴⁸ $\text{C}_6\text{H}_3(\text{NO}_2)_3$, picric acid, tetryl, $\text{C}_6\text{H}_2(\text{NO}_2)_3\text{NH}\cdot\text{CH}_2\cdot\text{NO}_2$, and liquid nitroglycerol, which decompose at much lower temperatures than would be expected from the observed energy of activation. With azides there is also another regularity. In some heterogeneous reactions it has been found that the rate of reaction per cm^2 of the catalyst is equal to νN , where N is the number of molecules per cm^2 and ν a factor having the dimensions of a frequency and a numerical value about 10^{13} sec^{-1} , i.e., a frequency comparable to that of the lattice. The decomposition of the azides falls within this category, and it might fairly be concluded that these decompositions are normal interface reactions. The existence of an induction period and the exponential rate-time character of the initial stage of the decomposition remain to be explained. Again, the period of induction may be attributed to the growth of nuclei. To explain the subsequent increase of rate, a conception current in

⁴⁷ J., 1936, 657.

⁴⁸ S. Z. Roginski, *Physikal. Z. Sovietunion*, 1932, 1, 649.

homogeneous reactions is employed.⁴⁹ Many oxidations, *e.g.*, the slow oxidation of hydrocarbons, exhibit a similar behaviour of reaction rate with time, and these reactions are known to be of the branching-chain type. By assuming that a similar general mechanism holds for solid reactions, without specifying the exact nature of the reaction centres, it is easy to derive an expression consistent with the experimental results. If N is the number of reaction centres generated per sec., and K is the number of times per sec. that two molecules are activated instead of one (*i.e.*, that the chain branches, in kinetic parlance), then

$$dN/dt = N_0 + KN$$

$$\text{or} \quad \ln N = Kt + \ln N_0/K.$$

Since N is proportional to the rate of increase of pressure

$$\ln dp/dt = Kt + \ln N_0/K.$$

Chains are terminated when they encounter a crack or molecules of the product of the reaction, which keeps the branching reaction in check. Unfortunately, the information obtained by such studies cannot give direct evidence of the nature of the chain propagators, but it would appear that some carriers do have a relatively long lifetime in that, should the reaction be stopped during the induction period by lowering the temperature, then on the crystals being reheated, the reaction starts where it left off. There are therefore some⁵⁰ who would oppose the chain hypothesis on these grounds, but in view of the close analogy with gaseous chain reactions, the corresponding reactions in solids cannot be so lightly dismissed in spite of lack of detail about the mechanism.

The mechanism of the dehydration of salt hydrates may be put into the same category, although there is a marked difference in that the reaction is strongly endothermic. The interesting observation is that the energy of activation for dehydration is practically equal to that of the heat change in the reaction for the copper sulphate hydrates. Hydration will therefore be a reaction of zero energy of activation. Again, the absolute rates are in agreement with those calculated from the simple theory (see p. 83) from the observed energy of activation. Observations by W. E. Garner and his co-workers⁵¹ on the rate of nuclear growth have shown that the energy of activation is practically the same as that for the evolution of water after the induction period. Individual variations in

⁴⁹ W. E. Garner and H. R. Hailles, *Proc. Roy. Soc.*, 1933, **A**, **139**, 588.

⁵⁰ See, *e.g.*, The Faraday Society Discussion, 1938, pp. 822—1082.

⁵¹ N. F. H. Bright and W. E. Garner, *J.*, 1934, 1372; W. E. Garner and W. Southon, *ibid.*, 1935, 1705; W. E. Garner and H. V. Pike, *ibid.*, 1937, 1565.

nuclear growth in different directions give rise to variety of nuclear shapes, but it is likely that the energy of activation is not greatly different in these directions. To explain the slow rate of nuclear growth, J. A. Cooper and W. E. Garner⁵² suggest that, owing to contraction of the solid, a negative tension is set up which reduces the vapour pressure and therefore the rate of evaporation.

Photo-processes in Solids.—Within the last few years a number of significant advances have been made in the photochemistry of solids. Absorption spectra of simple crystals with and without impurities may now be interpreted, some idea of the processes underlying fluorescence have been obtained, and a new light has been brought to bear on the theory of the photographic plate. The enlightenment is due to the application of the modern theory of solids to the problem and to the discovery of new facts in sufficiently simple systems.

We deal first with absorption spectra. Absorption in the visible and ultra-violet is due to excitation of electrons which may, as with free atoms, be raised to a discrete series of energy levels succeeded by a continuum representing ionisation. The discrete levels in the solid are blurred because of lattice vibrations and perturbation by crystalline fields. The blurring due to lattice vibrations can be diminished but not eliminated by working at low temperatures, as has been shown by J. T. Randall.⁵³ Exceptions to the above-mentioned behaviour occur when the absorbing groups are well screened from external influence. For example, compounds of the rare earths and transition elements, complex ions such as UO_2^{+} , and organic molecules containing conjugated double bonds have sharp energy levels in the solid state. In a solid, then, the criterion for ionisation is not a continuous broad band, but the onset of photoconductivity. Photochemical action may result from such excitation, but this phase of the subject will be omitted in this report.

Once the electron is excited to a discrete level, it either falls back to the ground level with the emission of radiation as fluorescence in some 10^{-8} sec., or the electronic energy is dissipated as heat and no radiation is emitted. In the former circumstance the fluorescent quantum is usually smaller than that absorbed, since electronic energy is partly dissipated as heat before fluorescence occurs. The decay of fluorescence follows the usual exponential law, $I = I_0 \exp(-\alpha t)$, where I_0 and I are the intensities at zero time and at time t respectively and α is a constant, since only one electron is concerned in the emission process. R. W. Gurney and N. F. Mott⁵⁴

⁵² *Trans. Faraday Soc.*, 1936, **32**, 1739.

⁵³ *Nature*, 1938, **142**, 113; cf. also C. J. Milner, *Trans. Faraday Soc.*, 1939, **35**, 101.

⁵⁴ *Ibid.*, p. 69.

have suggested another way in which electronic energy is used, *viz.*, to produce phosphorescence, one of the main characteristics being a much longer decay period than that of fluorescence. When in the discrete level the electron may receive energy from the lattice to raise it into a true continuous level or conduction band. The electron then moves away from its original position, leaving a positive hole behind. The electron may then be trapped in a bound energy level or it may combine eventually with a positive hole whereupon radiation is emitted. The intensity of emitted radiation will thus be proportional to the product of the concentration of holes and electrons, and hence the decay law will be of the second order.

Randall's observation that the intensity of fluorescence increases

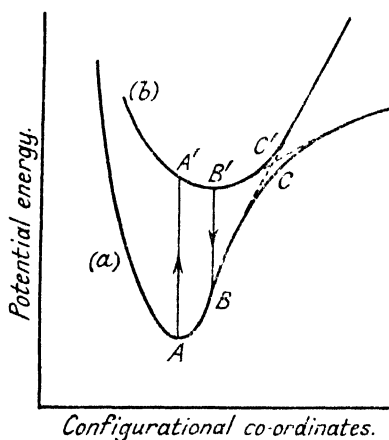


FIG. 7.

Potential-energy diagram of a crystal exhibiting fluorescence and phosphorescence.

with decreasing temperature among a number of pure substances, *e.g.*, manganese, lead, cadmium, and samarium salts, not exhibiting photo-conductivity, has suggested to Gurney and Mott a general mechanism for fluorescence which is best explained by means of a diagram. The potential energy of the absorbing centre may be represented for simplicity in a two-dimensional diagram as a function of configurational co-ordinates (Fig. 7). On absorption of a quantum, the Franck-Condon principle comes into operation, with the result that there is a vertical transition in the diagram to the upper excited state possessing considerable vibrational energy. This is lost to the lattice in a period of the order of a lattice vibration, *i.e.*, 10^{-13} sec., long before fluorescence occurs, in 10^{-8} sec. In consequence, a quantum of lower frequency is emitted. In order

to explain the temperature dependence, it is postulated that the potential-energy curves cross. At this point the excited state will have a high probability of reverting to the ground state with large vibrational energy, but without emission of radiation. In order to reach point *C*, however, energy must be acquired from the lattice. At low temperatures this is so infrequent an occurrence that nearly every absorbed quantum is emitted as a fluorescent quantum; at high temperatures fluorescence may not be detectable. Thus, under suitable conditions fluorescence may be a much more common phenomenon than was once supposed.

The most striking examples of the luminescence of solids are provided by those solids which from a chemical point of view are impure. Examples are calcium and zinc sulphides containing a variety of metallic sulphides. Many of these substances are of ill-defined chemical constitution and cannot be obtained in large crystals. R. Hilsch, R. W. Pohl, and their collaborators⁵⁵ have discovered that alkali halide crystals activated with small amounts (0.001—0.01%) of the corresponding thalious halide exhibit both fluorescence and phosphorescence and are, in general, systems more suitable for experimental work. The absorption spectrum of such crystals consists of broad bands lying at a longer wave-length than the first fundamental band of the pure alkali halide itself. With the chlorides there are three absorption peaks of the *A*, *B*, and *C* bands. For example, potassium chloride has its first fundamental band at 1636 Å., the *A*, *B*, and *C* bands lying at 2530, 2110, and 1976 Å. respectively. A systematic investigation has shown that the absorption maxima are practically independent of the cation in any one halide. The anion has a small effect, the iodides absorbing at a somewhat longer wave-length than the chlorides, the bromides being intermediate between the two. On irradiation there is no decomposition as with the pure thalious halide and there is no photo-conductivity. F. Seitz⁵⁶ therefore concludes that absorption is due, not to the halide ion, but to the thallium, and that the system is initially raised to a discrete level. No doubt, with light of short enough wave-length the electron might be raised into the conduction band. Two facts are in favour of this supposition. First, if the absorption were due to the halide, the bands should have a doublet structure, whereas none is shown;⁵⁷ secondly, absorption should lie further into the ultra-violet. The reason for the latter statement is that the halogen-thallium transition should lie close to the halogen-rubidium which is much further into the ultra-violet—

⁵⁵ For a summary, see R. Hilsch, *Proc. Physical Soc.*, 1937, **49**, 40.

⁵⁶ *J. Chem. Physics*, 1938, **6**, 150.

⁵⁷ R. W. Pohl, *Proc. Physical Soc.*, 1937, **49**, 5.

1684 Å. for rubidium chloride. In point of fact, the *C* band for RbCl(Tl) is at 1944 Å. If this assumption be made, it is possible to correlate the position of three absorption bands with the corresponding transitions in the free atom.⁵⁶

To simplify the discussion, reference will be confined to the potassium chloride phosphor. If light is absorbed in the *A*, *B*, or *C* bands, fluorescence is emitted in two superimposed bands lying on the long wave-length side of the absorption bands. Moreover, any absorption band is effective, the quantum efficiency is of the order of unity, and the relative intensities of the emission bands are independent of which excitation band is employed. Just as absorption spectra may be due to a multiplicity of levels in the crystal, so the fluorescent emission spectra may be accounted for by postulating suitable crossing of potential-energy curves, so that the system finally reaches a level such that either fluorescent band may be emitted.

The phosphorescence has rather different characteristics. Apart from the longer decay period, which is increased at lower temperatures, only light in the *B* and *C* bands is effective. Moreover, the intensity is proportional to the square of the intensity of the exciting radiation; the decay, however, follows a first-order equation and is quickened by infra-red radiation. The effect seems to be due⁵⁶ to the co-operation of two thallium ions producing such a condition that the system may reach a metastable region. Entry into that region is dependent on the square of the incident intensity; escape from it, at a rate proportional to the concentration of the metastable state, is facilitated by supply of energy from the lattice or by infra-red radiation. The existence of the metastable minimum thus ensures the production of phosphorescence owing to the tardy escape of energy by radiation.

A somewhat different state of affairs exists with zinc sulphide phosphors. Pure zinc sulphide, either wurtzite or blende, does not phosphoresce, but the disturbance produced by having the two crystal modifications in juxtaposition is sufficient to produce phosphorescence. Similarly, sulphides of copper, silver, etc., also induce phosphorescence. The criterion for the functioning of a sulphide activator seems simple. For example, lead sulphide will activate calcium and strontium sulphides but not zinc sulphide. By employing radioactive thorium-*B*—an isotope of lead—it can be shown that lead does not enter the zinc sulphide lattice.⁵⁸ In this manner interdiffusion of metallic sulphides may be followed by measuring the phosphorescent intensity of successive layers of phosphors.⁵⁹ The reason for the occurrence of diffusion into the

⁵⁸ H. Kading and N. Riehl, *Angew. Chem.*, 1934, **47**, 263.

⁵⁹ E. Tiede, *Ber.*, 1932, **65**, 364; N. Riehl, *Ann. Physik*, 1937, **20**, 654.

zinc sulphide lattice appears to be one of size. If the metallic atom can be accommodated without distortion in the vacant tetrahedra of the zinc sulphide lattice, diffusion and therefore phosphorescence are observed; if not, the energy of activation for diffusion is so high that it effectively stops that process.

Phosphorescence is optically an efficient process in spite of the fact that the absorption coefficient is unaltered by the addition of the activator. The energy acquired by the lattice must reach the activator without loss, for the impurity is on the average at least 20 atomic diameters away from the scene of absorption. A clue to the mechanism of emission is provided by the fact that, for some phosphors, the crystal exhibits photoconductivity, and that the rate of decay is of the second order, the velocity being temperature-dependent.⁶⁰ The second-order decay law certainly proves the participation of two particles in the emission process—photoconductivity shows that one is an electron. The other must be a positive hole left behind. The latter also may migrate in the sense that a neighbouring electron destroys it with the simultaneous creation of an adjacent positive hole. When positive hole and electron come together in presence of the activator, the function of the latter is to provide a discrete level by means of which the energy of combination of electron and positive hole may be emitted as radiation.

Besides the phenomenon of the transfer of energy in crystals, there is also an interesting example of the transfer of energy from the solid to the gas phase, discovered by H. Kautsky.⁶¹ Dyes such as porphyrin, tryptoflavin, and chlorophyll, when adsorbed on silica or alumina gel, absorb radiation and re-emit it without imparting any appreciable fraction to the support. In presence of oxygen, however, the fluorescence is quenched and the oxygen molecule is excited to a low-lying metastable level. Such oxygen molecules readily oxidise some substances, *e.g.*, leuco-malachite-green, in which the colour change is evidence of reaction. This may be demonstrated by mixing together gel particles containing the two dyes. In absence of oxygen the leuco-compound is unchanged. There is an optimum pressure for the effect — *ca.* 10^{-3} mm. At low pressures only a fraction of the energy is removed by the impact of the oxygen molecules, and at high pressures the metastable oxygen molecules are deactivated by collisions with normal molecules on diffusing to the leuco-compound.

H. W. M.

⁶⁰ A. L. Reimann, *Nature*, 1937, **140**, 501.

⁶¹ *Biochem. Z.*, 1937, **291**, 271.

5. IRREVERSIBLE ELECTRODE PROCESSES.

If an electrode reaction is carried out at an appreciable rate the electrode potential may be different from the reversible value. The reaction is then an irreversible one, and the electrode is said to be "polarised" or to exhibit an "overpotential." The overpotential at an electrode is defined as the potential difference between this electrode and a similar reversible electrode in the same solution. It is possible to distinguish three main causes of irreversibility.

Activation Overpotential, V_a .—Consider the general case of a dissolved ion which moves up to the electrode surface, is discharged, and finally evolved as an atom or molecule. The process may occur in several stages each of which may require a definite energy of activation, but it is clear that the reaction velocity will be controlled by the slowest of these stages, which is usually that requiring the highest energy of activation.

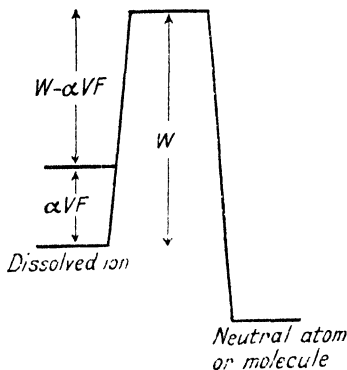


FIG. 8.

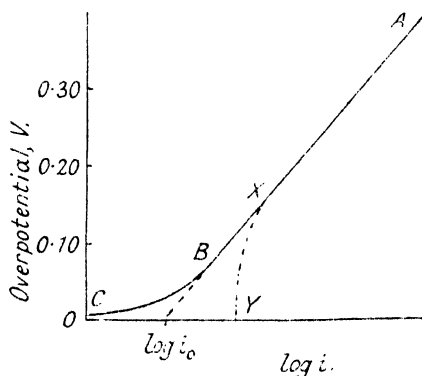


FIG. 9.

Let W be the energy of activation of the slowest stage when the electrode is at its reversible potential. We may expect that the energy of activation will be some function of the electrode potential. If the ion is negative, for example, the discharge will be facilitated by making the electrode more positive. If the overpotential is V , the alteration in the energy of activation will be αVF , where α represents this function, and the new energy of activation will be $W - \alpha VF$ (Fig. 8). Experiment has shown that for many reactions α is a constant.

If the distribution of energy among the reacting species is Maxwellian, the number reacting per second, N , is given by

$$N = N_0 e^{-(W - \alpha VF)/RT} \quad (1)$$

where N_0 is the number present at the electrode surface.³

If N is measured by the current density, i ,

$$\ln i = \text{const.} + \alpha VF/RT \quad . \quad . \quad . \quad (2)$$

$$\text{and } \partial \ln i / \partial V = 2.303 \partial \log i / \partial V = \alpha F/RT \quad . \quad . \quad (3)$$

so that the overpotential plotted against the logarithm of the current density should give a straight line the slope of which is equal to

$$\alpha F/2.303RT.$$

The height of the energy barrier ($W - \alpha VF$) may be obtained from the temperature coefficient of the current density ($C.D.$) (at constant overpotential) since

$$(\partial \ln N / \partial T)_V = 2.303 (\partial \log i / \partial T)_V = (W - \alpha VF)/RT^2 \quad . \quad (4)$$

or from the temperature coefficient of the overpotential (at constant $C.D.$) since

$$(\partial V / \partial T)_i = - (W - \alpha VF)/\alpha FT \quad . \quad . \quad . \quad (5)$$

It should be emphasised that the relations (2)–(5) are derived¹ without any particular assumptions as to mechanism. The only assumptions made are that some energy of activation is required, that this is influenced by the electrode potential, and that the energy distribution is Maxwellian.* This type of overpotential, which is due to the existence of a high energy of activation in the electrode reaction, may be called “activation overpotential,” V_a . The overpotentials of hydrogen and oxygen are of this kind.

The relation (2) may be written in the form :

$$V_a = b(\log i - \log i_0) \quad . \quad . \quad . \quad (6)$$

where b is equal to $2.303 RT/\alpha F$. Tafel² showed that the overpotential of hydrogen followed this equation. This relation is of very wide applicability, and is illustrated in Fig. 9. It will be seen that if the straight line, AB , corresponding to the experimental observations is extrapolated to $V_a = 0$ (i.e., to the reversible hydrogen potential in this solution), the intercept is equal to $\log i_0$; i_0 is thus the rate of deposition of hydrogen at the reversible potential. At this potential, however, the deposition of hydrogen is exactly balanced by the reverse process, viz., electro-solution of hydrogen; both processes have the velocity i_0 , so the net rate of deposition is zero.

At any potential the observed $C.D.$ is actually equal to the difference between the rate of deposition of hydrogen ions and the rate of electro-solution of hydrogen. In most cases the latter rate

¹ F. P. Bowden, *Proc. Roy. Soc.*, 1929, **A**, **126**, 107.

² J. Tafel, *Z. physikal. Chem.*, 1905, **50**, 641.

* Similar relations could be derived on the assumption that the potential change increased the current density by increasing the number of reacting particles on the electrode surface, and had no direct influence on the height of the energy barrier.

only becomes negligible in comparison with the deposition rate when the cathodic overpotential is greater than about 50 millivolts. At lower overpotentials the net *C.D.* is significantly less than the rate of deposition of ions. Since equations (1) and (5) apply to the rate of deposition alone, the observed net *C.D.* does not obey this law at low overpotentials. The experimental V - $\log i$ curve is no longer linear under these conditions (B' , Fig. 9).

It is evident that the rate of deposition at the reversible potential, i.e., i_0 , is the most useful measure of the catalytic activity of the electrode for this reaction. If i_0 is large, then the metal is an active one, and the overpotential is small. If i_0 and the constant b are known, it is easy to calculate the overpotential V_a at any current density i by means of equation (5); b is, of course, given by the slope, $\partial V / \partial \log i$, of the linear portion AB of the curve in Fig. 9.

The presence of very small traces of oxidising substances (in the case of hydrogen overpotential) or of reducing substances (in the case of oxygen overpotential) will cause V to fall below its theoretical value. This is particularly marked at low *C.D.*'s, and the curve may take the form AXY (Fig. 9). This form is frequently observed in solutions which have not been rigorously purified.

In the past, the variation of the overpotential with the current density has not been sufficiently appreciated. Many workers restrict their observations to the "minimum" overpotential. This is defined as the potential at which bubbles first appear on the electrode surface, or at which some supposed discontinuity is observed in the relation between current and potential. It is clear that this "overpotential" is characteristic of only one arbitrary *C.D.*, and the information it can give is limited.

*Concentration Overpotential, V_c .*³—The passage of current may cause a change in the concentration of the electrolyte close to the electrode at which reaction is taking place, and cause it to fall from C_0 to C_e . This concentration change may alter the reversible potential of this electrode. In practice the reference electrode is usually situated outside the region affected by concentration changes, so that the measured potential difference between the two electrodes, i.e., the overpotential, may include a term V_c where

$$V_c = (RT/nF) \ln C_e/C_0 \quad . \quad . \quad . \quad (7)$$

V_c may be called⁴ the "concentration overpotential."^{*}

³ See F. Foerster, "Elektrochemie wässriger Lösungen", Leipzig, 1922, for general review of earlier work.

⁴ J. N. Agar and F. P. Bowden, *Proc. Roy. Soc.*, 1938, A, **169**, 206.

^{*} In order to avoid the confusion which arises from the loose use of the word "polarisation," the term "concentration polarisation," which is sometimes used for potential changes of this nature, is not employed here.

When a steady state is reached, the rate of removal of an ion by deposition must be equal to the rate at which it is supplied from the bulk of the solution where its concentration is supposed to remain constant. The ion is supplied by (i) migration, (ii) convection, (iii) diffusion. It is difficult to give a complete solution of the hydrodynamical problems involved in the last two processes. It is therefore necessary to proceed by semi-empirical and approximate methods. In this connexion the concept of the diffusion layer^{5, 6, 9} has been found very useful. There can be no motion of fluid across the electrode surface itself, and therefore convection cannot take place at any point on this surface. On the other hand, in the bulk of the solution, at sufficiently large distances from the electrode, the concentration is practically uniform, and in this part of the system diffusion plays little part. On this basis it is considered that the electrode is covered with a "diffusion layer" of thickness δ . Outside this layer the concentration is that of the bulk of the solution. Inside the layer it is assumed that convection is negligible and that the reactant is supplied to the surface by diffusion and migration alone. The rate of diffusion through the layer, per sq. cm. of surface area, is equal to $k(C_0 - C_e)/\delta$, where k is the diffusion coefficient of the substance concerned. Since C_e cannot become less than zero, the rate of diffusion cannot exceed kC_0/δ . If the *C.D.* at an electrode is made to exceed this value (the limiting *C.D.*, i_l) the current must partly be carried by the deposition of some other ion. This will generally take place at a higher potential than the original process, and a sharp rise in the potential therefore occurs when the *C.D.* reaches the limiting value. Experimental determinations of δ generally rest on measurements of the limiting diffusion rate.

In *unstirred solutions* the motion of the liquid is mainly due to the density differences which accompany the concentration changes. For this reason δ varies slightly with the concentration difference, $(C_0 - C_e)$, but has a value about 0.05 cm. in most cases.^{6, 7} In *stirred solutions* δ decreases⁸ as the rate of stirring increases. It is usually of the order 0.001—0.005 cm.^{6, 8, 9} It can be shown

⁵ A. A. Noyes and W. R. Whitney, *Z. physikal. Chem.*, 1897, **23**, 689; W. Nernst, *ibid.*, 1904, **47**, 52; F. Weigert, *ibid.*, 1907, **60**, 513; T. R. Rosebrugh and W. Lash Miller, *J. Physical Chem.*, 1910, **14**, 816.

⁶ See S. Glasstone and A. Hickling, "Electrolytic Oxidation and Reduction," 1935, for a good general review.

⁷ R. E. Wilson and M. A. Youtz, *J. Ind. Eng. Chem.*, 1923, **15**, 603; S. Glasstone and G. D. Reynolds, *Trans. Faraday Soc.*, 1933, **29**, 399; S. Glasstone, *J.*, 1929, 690; *Trans. Electrochem. Soc.*, 1931, **59**, 277.

⁸ W. Nernst and E. S. Merriam, *Z. physikal. Chem.*, 1905, **53**, 235.

⁹ E. Brunner, *ibid.*, 1904, **47**, 56; 1906, **58**, 1.

theoretically that in stirred solutions δ is independent of the concentration difference.¹⁰

Some of the important differences between activation overpotential V_a and concentration overpotential V_c are set out below.⁴

(i) *Effect of stirring.* In the case of concentration overpotential the value of the limiting current i_l is always increased by stirring, so that V_c will fall. Stirring has little or no effect on V_a .

(ii) *The nature of the surface.* V_a is profoundly affected by the nature and physical state of the electrode surface; V_c is in general unaffected by these factors. If, however, the surface irregularities are very large so that they penetrate beyond the diffusion layer, they may cause small variations in V_c .

(iii) *Temperature coefficient.* Both V_a and V_c decrease as the temperature rises. The value of dV_a/dT varies, of course, from one reaction to another, but for a number of reactions in aqueous solution, it is *ca.* 2 or 3 millivolts per degree; $-dV_c/dT$ is smaller, since it depends on the temperature coefficient of diffusion and is usually a fraction of a millivolt per degree.

(iv) *Current density.* V_a is proportional to the logarithm of the C.D. (equation 6). The relation between V_c and the C.D. is usually different from this.

(v) *Rate of growth.* V_a grows rapidly when the current is switched on. The potential change is proportional to the quantity of electricity passed, and the electrode has a capacity of *ca.* 20 microfarads per sq. cm.¹¹ The growth of V_c is in most cases much slower, the potential does not change linearly with the quantity of electricity passed, and the apparent "capacity" is usually several thousand microfarads per sq. cm.⁴

Resistance Overpotential.—If there is an appreciable resistance between the solution and the electrode, the passage of the current will produce a potential drop across this resistance which may obey Ohm's law. We may call this the "resistance overpotential," V_r . The resistance may be due to the electrolyte itself, either because it is dilute or because local concentration changes have made it so near the electrode. In other cases it may be due to a poorly conducting oxide or other film on the surface of the electrode. These films occur, for example, on aluminium anodes.¹³

Since the resistance is often a complex function of i , the relation between V_r and i is not simple. If i is large, V_r may reach very high values indeed. A distinguishing characteristic of V_r is that it should, in general, cease the instant the current is switched off.

¹⁰ J. N. Agar, Diss., Cambridge, 1938.

¹¹ See, e.g., A. Frumkin, *Act. sci. ind.*, **373**, Paris, 1936.

The decay of V_a , though rapid, is exponential.¹² The decay of V_c is usually slower than that of V_a . Many investigations of the anodic formation of oxide and other films have been made. This work has been summarised by U. R. Evans,¹³ and we do not deal further with this subject here.

It is clear that all three types may occur simultaneously and the measured overpotential may be made up of $V_a + V_c + V_r$. It is not always easy to separate them experimentally, and much work is complicated by the fact that no clear distinction is made between the various causes of irreversibility.

The Electrodeposition of Hydrogen.—The electrodeposition of hydrogen from aqueous solutions is nearly always a highly irreversible process; it is only in exceptional cases, e.g., on platinised platinum or other specially active electrodes, that the reaction can occur at an appreciable rate without a large overpotential. At a given *C.D.* this hydrogen overpotential, on most metals, may show wide and uncontrolled variations according to the physical state and degree of contamination of the surface. This irreproducibility affects all solid metals and is probably greatest on the catalytically active metals.

It is possible, however, to obtain reproducible results on mercury surfaces and on other liquid surfaces such as gallium and Wood's alloy.¹⁴ If high currents are used, the overpotential includes terms due to V_a , V_c , and V_r . If the *C.D.* is kept low, however, V_c and V_r become negligibly small and the irreversibility is essentially due to *activation overpotential*. The use of small currents makes it imperative that traces of dissolved oxygen or other impurities should be removed from the solution (see *XY*, Fig. 9).

Mercury cathode. Experiment 1, 2, 15–17 has shown that in acid solutions the relation between the overpotential and the logarithm of the current (equation 6) holds for currents of 10^{-7} to 10^{-3} amp./cm.². If high currents are used, deviations occur.¹⁸ If, however, the solution is violently stirred or is in rapid motion so that concentration changes are prevented, the relation may hold good for

¹² F. P. Bowden and E. K. Rideal, *Proc. Roy. Soc.*, 1928, A, **120**, 59.

¹³ "Metallic Corrosion, Passivity and Protection," 1937, pp. 13 ff., 42 ff.; see also J. A. V. Butler and J. D. Pearson, *Trans. Faraday Soc.*, 1938, **34**, 806.

¹⁴ F. P. Bowden and E. A. O'Connor, *Proc. Roy. Soc.*, 1930, A, **128**, 318.

¹⁵ F. P. Bowden and E. K. Rideal, *ibid.*, 1928, A, **120**, 59.

¹⁶ S. Lewina and V. Sarinsky, *Acta Physicochim. U.R.S.S.*, 1937, **6**, 491.

¹⁷ F. P. Bowden and H. F. Kenyon, *Nature*, 1935, **135**, 105; H. F. Kenyon, *Diss.*, Cambridge, 1937.

¹⁸ F. P. Bowden, *Trans. Faraday Soc.*, 1928, **24**, 473.

much higher *C.D.*'s.¹⁹ At currents below 10^{-7} amp./cm.², the overpotential usually falls below its theoretical value. Recent experiments have shown that, if the cathode is completely enclosed and the polarising current is passed through the glass walls so that all traces of oxygen are excluded, the theoretical relationship is obeyed down to currents of 10^{-9} or 10^{-10} amp./cm.².²⁰

In acid solutions at room temperature $b = 0.120$ volt,^{1, 2, 15-18, 21} provided the electrode is not contaminated. Since $b = 2.303 RT/\alpha F$, $\alpha = 0.5$. Experiments carried out at different temperatures^{1, 2} show that b is proportional to the absolute temperature, so α is independent of temperature. As will be shown later, this value of α (*ca.* 0.5) is found for a large number of metals and also for the deposition of oxygen from acid solutions.

The deposition of hydrogen from alkaline solutions on to mercury is complicated by the simultaneous deposition of sodium and the formation of amalgam, and little work has been done in this field, but it has recently been shown¹⁷ that amalgam formation is unimportant at very low currents and equation (5) is again obeyed. The value of α is, however, different. In alkaline solutions (N/5-sodium hydroxide) $\alpha = ca.$ 0.25, which is *one half of the value found in acid solutions under similar conditions*. This low value of α has also been observed in buffered solution of p_H 0.8—6.6.¹⁸ At low currents $\alpha = 0.5$, but on increasing the current a break occurs and the slope of the line changes so that α now has a value of 0.25. The current at which this break occurs becomes progressively lower as the p_H is increased. It seems probable that this change is due to the fact that the buffering agents fail to prevent the solution near the cathode from becoming alkaline at high currents.* These experiments suggest that the mechanism of deposition in alkaline solution is different from that in acids.

Several investigators^{16, 23, 24} have studied the effect of changes of p_H on the overpotential in acid solutions. According to the theory developed by A. Frumkin²⁵ (see below) the overpotential should be independent of the p_H in pure acid solutions, but should

¹⁹ B. Kabanov, *Acta Physicochim. U.R.S.S.*, 1936, **5**, 193; *J. Phys. Chem. Russia*, 1936, **8**, 486.

²⁰ F. P. Bowden and K. E. Grew, in course of publication; K. E. Grew, *Diss.*, Cambridge, 1936.

²¹ E. Baars, *Sitzungsber. Ges. Beförd. Naturwiss. Marburg*, 1928, **63**, 213; E. Baars and C. Kayser, *Z. Elektrochem.*, 1930, **36**, 429.

²² *Acta Physicochim. U.R.S.S.*, 1937, **7**, 485.

²³ S. Glasstone, *J.*, 1924, **125**, 2646.

²⁴ J. Heyrovsky, *Rec. Trav. chim.*, 1925, **44**, 499; P. Heyrasymenko, *ibid.*, p. 503.

²⁵ *Z. physikal. Chem.*, 1933, **A**, **164**, 121.

* But see Lewina and Sarinsky.²²

become 0.058 volt greater (more negative) for each ten-fold decrease in the hydrogen-ion concentration, if a large excess of a foreign electrolyte is present. In agreement with this, S. Lewina and V. Sarinsky^{16, 22} have found that the overpotential is the same in 0.01, 0.1, and 1.0N-hydrochloric acid, but increases by 0.04—0.05 volt per ten-fold decrease in hydrogen-ion concentration in similar solutions containing an excess of lanthanum chloride. On the other hand, Bowden^{1, 18} found that the overpotential was independent of p_H at low *C.D.*'s in *buffered* solutions containing a large quantity of foreign electrolytes. Recent experiments of C. Wagner and W. Traud²⁶ in acid solutions of various p_H , but all M with respect to calcium chloride, also indicate a much smaller change in the overpotential than Frumkin's theory requires. Although the present position is not very satisfactory, the experimental evidence shows that in most cases the overpotential is practically independent of the p_H , provided it is not too high. This is in general agreement with earlier work.^{2, 23}

The height of the energy barrier can be determined from the temperature coefficient of the overpotential or of the *C.D.*¹ (equations 3 and 4). Experiment shows that both these relations give the same result. The values of the energy of activation obtained in this way are given in Table I.

Overpotential of hydrogen isotopes. After the discovery and development of the electrolytic method for preparing heavy water,^{27, 28} many measurements of the isotopic separation factor (*S*) were reported;²⁹ the results were extremely divergent. It was pointed out by R. H. Fowler³⁰ that the fractionation could not be due to a difference in the ionic mobilities of the isotopes, but must be caused by the difference in the speeds at which the isotopes react at the cathode. A comparison by Bowden and Kenyon¹⁷ of the overpotentials of hydrogen and deuterium showed that they differed by an amount which was adequate to account for the observed separation factors.

The kinetics of electrodeposition from 0.2N-sulphuric acid on a mercury cathode were very similar for both isotopes ($\alpha = 0.52$ in each case) but the overpotential of deuterium was considerably higher than that of hydrogen. At a given *C.D.* the cathode potential for deuterium was 0.115 volt more negative (on the saturated

²⁶ *Z. Elektrochem.*, 1938, **44**, 391.

²⁷ E. W. Washburn and H. C. Urey, *Proc. Nat. Acad. Sci.*, 1932, **18**, 496.

²⁸ G. N. Lewis and R. T. MacDonald, *J. Chem. Physics*, 1933, **1**, 341.

²⁹ *Ann. Reports*, 1934, **31**, 13; H. C. Urey and G. K. Teal, *Rev. Mod. Physics*, 1935, **7**, 34; J. A. V. Butler, *Z. Elektrochem.*, 1938, **44**, 55.

³⁰ *Proc. Roy. Soc.*, 1934, **A**, **144**, 452.

calomel scale at 25°). This difference in overpotential means that the electrodeposition of hydrogen from light water thus occurs about ten times faster than the deposition of heavy hydrogen from heavy water at the same cathode potential. The measurement of the temperature coefficient shows that the respective energies of activation are 18.0 kg.-cals. for hydrogen and 20.9 kg.-cals. for deuterium. In 0.2N-potassium hydroxide solution α is 0.24 in each case and the cathode potential (on the saturated calomel scale) of the deuterium at any given current is 0.159 volt more negative. The energies of activation W in alkaline solution are 8.65 kg.-cals. for hydrogen and 10.7 kg.-cals. for deuterium. Later measurements by J. Novak³¹ on a dropping-mercury cathode in acid gave a difference in the cathode potentials of 0.087 volt at 20° and 0.071 volt at 60°, but this should be contrasted with the work of J. Heyrovský and O. H. Müller.³²

Investigations of separation coefficients under carefully controlled conditions have been made by J. Horiuti and G. Okamoto³³ and by H. F. Walton and J. H. Wolfenden.³⁴ The former point out that cathodes of nickel, gold, silver, copper, platinum, and lead (with alkaline electrolyte) all give values of S about 6, and that tin, mercury, and lead (with acid electrolyte) give values of 3.1, 3.1, and 3.0 respectively. Walton and Wolfenden confirm this division of cathodes with two groups. With silver, platinum, and nickel they find values of S at room temperature of 5—7, falling considerably with increase of temperature. With mercury and tin, S is about 3; in the case of mercury it falls slightly with rising temperature, and in that of tin there is actually an increase of S with temperature. With the exception of this anomalous behaviour of tin, the results are in agreement with the theory of Horiuti and Okamoto (see p. 104).

Other metals. Numerous experiments show that the logarithmic relation (6) between overpotential and $C.D.$ holds true for the deposition of hydrogen on most metals.^{1, 2} Some typical results of recent work with different metals are collected in the following table. As previously stated, the activity of solid electrodes varies considerably, so the results are not always reproducible.

In this table α is obtained experimentally from the slope of the V - $\log i$ curve; i_0 is obtained by extrapolating this curve to $V = 0$ and is a measure of the rate of deposition when the overpotential is zero. The energy of activation W is calculated from

³¹ *Coll. Czech. Chem. Comm.*, 1937, **9**, 207.

³² *Ibid.*, 1935, **7**, 281.

³³ *Sci. Papers Inst. Phys. Chem. Res. Tokyo*, 1936, **28**, 231.

³⁴ *Trans. Faraday Soc.*, 1938, **34**, 436; *Nature*, 1936, **138**, 468.

TABLE I.

*The Overpotential of Hydrogen on Different Metals.**

Electrode.	Solution.	$\alpha = \frac{2.303RT}{bF}$	i_0 , amp./sq. cm.	W , kg.-cals.	Remarks.	Reference.
Mercury	0.2N-H ₂ SO ₄	0.52	6×10^{-12}	18.0	25°	17, cf. 1
	0.2N-D ₂ SO ₄	0.52	0.8×10^{-12}	20.9	25°	17
	0.1N-HCl	0.49	1.7×10^{-12}	—	25°	16
	0.2N-NaOH	0.24	6.9×10^{-3}	8.65	25°	17
	0.2N-NaOD	0.24	2.3×10^{-3}	10.7	25°	"
	0.35N-HCl	0.4—0.5	10^{-11}	—	—	20
	in MeOH 0.01—0.5N-HCl in EtOH	0.5	2×10^{-11}	—	—	35
Gallium	0.2N-H ₂ SO ₄	0.5	1.6×10^{-7}	15.2	87°	14
Wood's alloy	"	0.4	1×10^{-8}	16.4	87°	"
Polished Ag	"	0.5	3.2×10^{-8}	—	25°	15
Etched Ag	"	0.5	6×10^{-7}	—	—	"
Nickel	"	0.52	6×10^{-7}	—	25°; i_0 very dependent on state of surface	"
Bright platinum †	"	0.75—0.3	$1.4—6 \times 10^{-6}$	9.5—11.5	α decreases with time	1, 36
Spongy platinum	"	—	ca. 10^{-3}	—	—	1
Bright platinum	0.2N-NaOH	0.8—0.5	$0.1—2 \times 10^{-6}$	6—7	22°; i_0 very dependent on state of surface	37
Palladium	N-KOH	0.5	ca. 10^{-3}	—	—	38
	N-H ₂ SO ₄	1.2—0.5	$0.1—5 \times 10^{-1}$	—	Activated by anodic oxidation	39
Palladium	0.2N-H ₂ SO ₄	0.5	2×10^{-5}	9	Electrode cleaned by flaming	42
Lead	0.2N-NaOH	0.4—0.5	1×10^{-5}	10	" "	37
	2N-H ₂ SO ₄	0.3	—	—	" "	43
Tantalum	2N-H ₂ SO ₄	0.28	—	—	" "	11
Copper	—	0.8—0.5	10^{-5} to 10^{-6}	—	" "	44
Bismuth	"	0.5—0.4	5×10^{-12} to 8×10^{-11}	—	Results variable; surface possibly contaminated	45
Cobalt	"	0.5 (falling)	10^{-8}	—	" "	"
Antimony	"	0.2 (variable)	2×10^{-6}	—	" "	"
Carbon	"	0.5	10^{-11}	—	—	43

* Some further values of α (or b) are given in a useful review by K. Wirtz.⁴⁵

† Values of α as large as 2 have been observed on particularly active Pt and Pd electrodes.^{40, 41, 47} It seems probable that the overpotential in these cases is concentration overpotential, due to the change in concentration of dissolved hydrogen near the electrode.⁴⁰

³⁵ S. Lewina and M. Silberfarb, *Acta Physicochim. U.R.S.S.*, 1938, **4**, 275.

³⁶ M. Volmer and H. Wick, *Z. physikal. Chem.*, 1935, **A**, **172**, 429.

³⁷ F. P. Bowden and J. N. Agar, unpublished; J. N. Agar, Diss., Cambridge, 1938.

³⁸ G. Masing and G. Laue, *Z. physikal. Chem.*, 1936, **A**, **178**, 1.

³⁹ C. A. Knorr and E. Schwartz, *Z. Elektrochem.*, 1934, **40**, 38; *Z. physikal. Chem.*, 1936, **A**, **176**, 161.

⁴⁰ L. Kandler and C. A. Knorr, *Z. Elektrochem.*, 1936, **42**, 669; L. Kandler, C. A. Knorr, and C. Schwitzer, *Z. physikal. Chem.*, 1937, **A**, **180**, 281.

⁴¹ M. G. Raeder and K. W. Nilsen, *Chem. Zentr.*, 1935, ii, 3640; *Norges Tekn. Høiskole Avhandl.*, Til 25 års Jubileet, 1935, 263.

⁴² F. P. Bowden and H. P. Stout, unpublished.

⁴³ T. Erdey-Grúz and H. Wick, *Z. physikal. Chem.*, 1932, **A**, **162**, 53.

⁴⁴ K. Wirtz, *ibid.*, 1937, **B**, **36**, 435.

⁴⁵ F. P. Bowden and L. E. Price, unpublished.

⁴⁶ L. P. Hammett *et al.*, *J. Amer. Chem. Soc.*, 1924, **46**, 7; 1925, **47**, 1215; 1933, **55**, 70.

⁴⁷ L. P. Hammett, *Trans. Faraday Soc.*, 1933, **29**, 770.

⁴⁸ *Z. Elektrochem.*, 1938 **44**, 303.

the temperature coefficient of overpotential (equation 4 or 5). The characteristic overpotential on the metal at any *C.D.* can be obtained from the values of i_0 and α in this table. For example, the overpotential in acid solution on a mercury cathode at a current of 10^{-5} amp./cm.² and at 25° is

$$\begin{aligned} V &= 2.303 \frac{RT}{\alpha F} (\log i - \log i_0) \\ &= \frac{2.303 \times 8.31 \times 298}{0.5 \times 96,500} [\log (10^{-5}) - \log (6 \times 10^{-12})] \\ &= 0.72 \text{ volt} \end{aligned}$$

In acid solution the majority of the metals give $\alpha = ca. 0.5$ when the surface is clean. The notable exceptions to this are platinum and palladium. On these metals α may be initially very high^{21, 37, 39, 41} (*ca.* 1) and may fall with time.^{1, 39} The value of α is greatly influenced by traces of contaminants such as arsenious oxide. On lead, cobalt, and antimony, α is low and variable.

It will be seen that i_0 varies over a wide range on the different metals. For a high-overpotential metal, *e.g.*, mercury, i_0 is as small as 10^{-12} to 10^{-11} amp./cm.²; for a low-overpotential metal, *e.g.*, palladium, it may be as large as 10^{-5} to 10^{-4} amp./cm.². On specially "activated" surfaces the value may be higher still.⁴⁰ The results for etched and for polished silver¹⁵ show clearly that i_0 is also influenced by the physical state of the surface. This makes it difficult to compare the overpotentials of different metals. If the electrodes are liquid, this difficulty is removed and experiment shows that, at the same temperature and overpotential, hydrogen is deposited some 30 times faster on gallium than it is on mercury.¹⁴ The increase in i_0 on solid surfaces which have been "activated" is partly due to an increase in the real accessible area of the electrode.¹⁵ The height of the energy barrier varies from 18 kg.-cals. (20.9 kg.-cals. for deuterium) on mercury, down to less than half this value on the low-overpotential metals such as platinum. It is interesting to note that the overpotential of hydrogen in *alcoholic* solutions is nearly the same as that observed in aqueous solutions.

Several authors^{36, 39, 46} have investigated the deposition of hydrogen on the catalytically active metals at low overpotentials, where the logarithmic relation breaks down. Volmer and Wick³⁶ find a roughly linear relation between current and potential near the reversible potential (platinum, gold, and iridium electrodes). In addition, they observed that at potentials considerably more *positive* than the reversible value, the *electrosolution* of hydrogen on platinum approximately obeys a logarithmic relation analogous to (6). But this behaviour does not seem to be general,^{39, 46} and there

is little doubt that the characteristics of the reaction at low overpotentials and in the anodic range depend markedly on the previous treatment of the electrode.

F. P. Bowden^{15, 49} has measured the quantity of electricity required to change the potential of a platinum electrode from the reversible hydrogen to the reversible oxygen potential. This quantity is sufficient to remove a unimolecular film of hydrogen and deposit a unimolecular film of oxygen on the electrode surface. J. A. V. Butler and G. Armstrong,⁵⁰ using the same method, find a similar result (see also J. A. V. Butler and J. D. Pearson⁵²). Frumkin and others⁵¹ have measured the amount of hydrogen adsorbed at various potentials and also the adsorption of ions in the double layer. They find that the chemical potential of the adsorbed hydrogen is proportional to the amount adsorbed, and that the quantity of hydrogen adsorbed at the reversible potential again corresponds to a complete monolayer. This interesting work also shows that hydrogen is more strongly adsorbed from alkaline than from acid solutions.

The overpotential of both hydrogen and oxygen is decreased when ultra-violet light falls on the electrode surface.⁵³ The magnitude of the photo-current increases with the overpotential and with the frequency of the light. Its effect is due, not to electron emission, but to an acceleration of the surface reaction.⁵³ Ultra-violet light will also liberate hydrogen from various aqueous solutions, and some separation of the isotopes may be effected in that way.⁵⁴

The Overpotential of Oxygen.—The deposition of oxygen cannot be studied on most metals because the metal dissolves or is attacked by the oxygen. Bowden¹ showed that the kinetics of electro-deposition of oxygen from acid solution on to a platinum anode closely resembles that of hydrogen on other metals. The overpotential was high and equations (3), (4), and (5) were obeyed; α was again equal to 0.5, $i_0 = 3.7 \times 10^{-11}$ amp./sq. cm. at 14°, and the energy of activation $W = 18.7$ kg.-cals.

⁴⁹ *Proc. Roy. Soc.*, 1929, A, **125**, 446.

⁵⁰ *Ibid.*, 1932, A, **137**, 604; J. A. V. Butler, G. Armstrong, and F. Himsworth, *ibid.*, 1933, A, **143**, 89.

⁵¹ A. Frumkin and A. Slygin, *Compt. rend. Acad. Sci. U.R.S.S.*, 1934, **2**, 167; *Acta Physicochim. U.R.S.S.*, 1935, **3**, 791; A. Slygin and W. Medwedowsky, *ibid.*, 1936, **4**, 911; A. Frumkin and A. Slygin, *ibid.*, 1936, **5**, 819; B. Erschler and M. Proskurnin, *ibid.*, 1937, **6**, 195; B. Erschler, *ibid.*, 1937, **7**, 327; B. Erschler, G. Deborin, and A. Frumkin, *ibid.*, 1935, **8**, 565.

⁵² *Trans. Faraday Soc.*, 1938, **34**, 1163.

⁵³ F. P. Bowden, *ibid.*, 1931, **27**, 505.

⁵⁴ A. Farkas and L. Farkas, *ibid.*, 1938, **34**, 1113, 1120.

T. P. Hoar⁵⁵ found that this relation also held for alkaline solutions and for the reverse process, the electro-solution of oxygen, although α was not always 0.5. F. P. Bowden and H. W. Keenan⁵⁶ found that α on a platinum anode was *ca.* 0.54 in very dilute alkaline solutions but increased steadily as the hydroxyl-ion concentration increased, reaching a value of 1.74 in 14N-sodium hydroxide. In solutions of sodium hydroxide the overpotential decreased as the hydroxyl-ion concentration increased, but in solutions of sulphuric acid it was independent both of p_H and of the sulphate-ion concentration. V. Vitek⁵⁷ finds that on a dropping-mercury electrode the electro-reduction of dissolved oxygen occurs in two stages. He attributes these to the reduction to hydrogen peroxide and thence to water.*

The overpotential of the halogens is usually very small unless high currents are used.^{56, 58} Much of the experimental work is complicated by the fact that concentration overpotential becomes important at high *C.D.*'s (see p. 109).

Overpotential of Metals.—It has been known for some time that the deposition of metals is accompanied by an overpotential which is usually small (a few millivolts) except for the transition elements iron, cobalt, and nickel,⁵⁹ for which it is quite large. Except in the case of mercury it is not due entirely to concentration changes. The discharged metal ions eventually find their way into the crystal lattice and the intermediate stages are not clearly understood. The kinetics of deposition have been investigated by T. Erdey-Grúz and M. Volmer.^{60, 61} If the discharge of the ion is the slow process the relation between overpotential and current will be similar to equation (6). If the discharge is rapid the slow process may be the incorporation of the ions into the crystal lattice. There is evidence that deposition only occurs at certain active centres. If the number of these active centres is constant, there will be a linear relation between the *C.D.* and the overpotential. If fresh active centres are continually being formed the relation will be more complex.

⁵⁵ *Proc. Roy. Soc.*, 1933, **A**, **142**, 628; see also W. Roiter and R. Jampolskaja, *Acta Physicochim. U.R.S.S.*, 1937, **7**, 47.

⁵⁶ Unpublished; see also H. W. Keenan, *Diss.*, Cambridge, 1936.

⁵⁷ *Coll. Czech. Chem. Comm.*, 1935, **7**, 537.

⁵⁸ F. Chang and H. Wick, *Z. physikal. Chem.*, 1935, **A**, **172**, 448.

⁵⁹ N. Thon, *Compt. rend.*, 1932, **197**, 1312; W. Roiter and W. Jusa, *Acta Physicochim. U.R.S.S.*, 1936, **4**, 135; see S. Glasstone, "Electrochemistry of Solutions," 1937, p. 452, for refs. to earlier work.

⁶⁰ *Z. physikal. Chem.*, 1931, **A**, **157**, 165.

⁶¹ T. Erdey-Grúz, *ibid.*, 1935, **A**, **172**, 157; T. Erdey-Grúz and E. Frankl, *ibid.*, 1936, **A**, **178**, 266; T. Erdey-Grúz and R. Kardos, *ibid.*, p. 255.

* See also *Ann. Reports*, 1937, **34**, 110.

Erdey-Grúz and Volmer⁶⁰ find that at low currents the relation is linear and that deviations occur at high currents. They consider that overpotential is due to the slow migration of ions to the active centres. This has been criticised by B. Hunt,⁶² who considers that the metal ions accumulate in the double layer until a continuous lattice can be formed over the face of a particular crystal. J. Hoekstra⁶³ observed that the linear relation holds good for high *C.D.*'s if the electrode is continuously scraped. He also found that deposition on most metals took place in layers of *ca.* 1000 atoms in thickness * except in the case of iron, nickel, and cobalt, in which small nodules were formed. E. Müller and H. Borchman⁶⁴ find that the deposition is affected by the nature of the anion. Satisfactory growth of single crystals is only obtained in a solution of complex salts.

Theories of Hydrogen Overpotential.—The deposition of hydrogen must occur in several stages. The H_3O^+ ion moves up to the cathode, loses its charge, combines with another hydrogen atom, and escapes from the surface as gaseous hydrogen. Each of these stages may be slow, but it is probable that the controlling stage is either (a) the neutralisation of the ion or (b) the formation of the H-H bond of the molecule H_2 . Either of these may have a large energy of activation. It was at one time thought that stage (a) would in all cases be rapid, and attention was concentrated on (b) as the rate-determining process responsible for the hydrogen overpotential.

(1) In its simplest form this mechanism^{2, 65} (the "Tafel" or "catalytic" mechanism) postulates that the slow stage of the reaction is the recombination of atoms adsorbed on the electrode surface. It is assumed that the rate of recombination is equal to kn^2 , where n is the number of adsorbed atoms per sq. cm. It is further supposed that the overpotential V is given by $V = (RT/F) \ln n/n_0$, where n_0 is the number of adsorbed atoms per sq. cm. at the reversible potential. Combination of these equations leads to the relation

$$i = kn^2 = kn_0^2 \cdot e^{2VF/RT} = i_0 \cdot e^{2VF/RT} \quad . \quad . \quad (7)$$

or to

$$i = i_0 (e^{2VF/RT} - 1) \quad . \quad . \quad . \quad (8)$$

if we take account of the fact that the actual observed current i is equal to the rate of recombination less the rate of spontaneous dissociation into atoms.⁶⁵ The latter is supposed to be independent

⁶² *Trans. Electrochem. Soc.*, 1934, **65**, 95.

⁶³ *Rec. Trav. chim.*, 1931, **50**, 339.

⁶⁴ *Z. Elektrochem.*, 1933, **39**, 341.

⁶⁵ *Ibid.*, 1934, **40**, 38.

* Cf. Erdey-Grúz and Volmer.⁶⁰

of the potential and is equal to i_0 . At high overpotentials the two expressions (7) and (8) are indistinguishable. According to this simple theory $\alpha = 2$; this is contrary to experiment in nearly all cases. The assumptions made in this treatment will break down, however, if the surface is approaching saturation with adsorbed hydrogen,⁶⁶ particularly if there are considerable repulsive forces between the adsorbed atoms. Under these conditions α can be much less than 2, and, in fact, tends to zero for a completely saturated surface.

Horiuti and his co-workers⁶⁶ have given a detailed treatment of the kinetics of recombination of adsorbed hydrogen atoms on a nickel electrode, by the transition state method, taking into account the varying degree of occupation of the surface, and the repulsive forces between the adsorbed atoms.

Another mode of formation of hydrogen molecules has recently been considered by the same authors.^{33, 66} This is the reaction between a hydrogen atom, adsorbed on the negatively charged electrode, and a hydrogen ion in solution: $\text{H}_3\text{O}^+ + \text{H-Me} \longrightarrow \text{H}_2 + \text{H}_2\text{O} + \text{Me}$. This so-called "electrochemical" mechanism has certain points in common with the earlier theories of Bowden¹ and of J. Heyrovský.⁶⁷ A thorough statistical mechanical treatment of this mechanism has also been given by J. Horiuti *et al.*⁶⁸ and G. Okamoto.⁶⁹

In the last ten years the view that the neutralisation of the H_3O^+ ion may be the rate-determining process has been developed, in slightly different forms, by several authors.⁷⁰⁻⁷⁴ According to R. W. Gurney's⁷¹ theory, the H_3O^+ ions in the solution near the cathode (within a few Å.) are neutralised by electrons from the metal which "leak" through the potential barrier at the surface, forming free hydrogen atoms and water molecules. This process is highly endothermic, and the energy of activation is in the first place due to this fact. It is increased by the high repulsive potential energy of the neutral complex H_2O which is the initial product of neutralisation. Gurney calculates the probability that an electron

⁶⁶ G. Okamoto, J. Horiuti, and K. Hirota, *Sci. Papers Inst. Phys. Chem. Res. Tokyo*, 1936, **29**, 223.

⁶⁷ *Rec. Trav. chim.*, 1925, **44**, 499; 1927, **46**, 582.

⁶⁸ *Bull. Chem. Soc. Japan*, 1938, **13**, 216.

⁶⁹ *J. Fac. Sci. Hokkaido Imp. Univ.*, 1937, (iii), **2**, 115.

⁷⁰ M. Volmer and T. Erdey-Grúz, *Z. physikal. Chem.*, 1930, **A**, **150**, 203.

⁷¹ *Proc. Roy. Soc.*, 1931, **A**, **134**, 137; *Physikal. Z. Sovietunion*, 1933, **4**, 360; R. H. Fowler, *Trans. Faraday Soc.*, 1932, **28**, 368.

⁷² *Z. physikal. Chem.*, 1932, **A**, **160**, 116.

⁷³ *Acta Physicochim. U.R.S.S.*, 1935, **2**, 505.

⁷⁴ *Proc. Roy. Soc.*, 1936, **A**, **157**, 423; see also *Trans. Faraday Soc.*, 1924, **19**, 734; 1932, **28**, 379.

and a hydrogen ion between them have sufficient energy for this process, and shows that this quantity, which is proportional to the *C.D.*, is an exponential function of the potential. It is also possible to explain why α is commonly equal to 0.5 on this basis. On the other hand, B. Topley and H. Eyring⁷⁵ have pointed out that this theory leads to an impossibly high energy of activation. It also suggests that the overpotential should be practically independent of the nature of the electrode,⁷⁶ whereas experiment shows that this is not the case.

The other neutralisation theories all postulate an adsorbed hydrogen atom instead of a free atom as the product of the reaction. As the heat of adsorption of hydrogen atoms on metals is usually considerable, this reaction is much "easier" than the production of free hydrogen atoms, and the difficulty with regard to the energy of activation disappears. A. Frumkin⁷² pointed out that this process can be regarded as a proton jump from the acid H_3O^+ to the negatively charged metallic surface, which behaves as a base in the generalised sense of J. N. Brönsted.⁷⁷ The fractional value of α is analogous to the fractional exponent in Brönsted's relation⁷⁸ connecting the catalytic constants of various acids with their dissociation constants. This view has been developed by J. Horiuti and M. Polanyi.⁷³ They consider the case of deposition on a nickel surface, and construct Morse functions giving the potential energy $\text{H}_3\text{O}^+-\text{H}$ and the Ni-H bonds in terms of the respective nuclear separations. It is assumed that the height of the energy barrier is given by the height of the point of intersection of the two Morse curves. This clearly depends on the separation of the H_3O^+ ion from the surface, but, using a reasonable value for this quantity, Horiuti and Polanyi find that the energy of activation at the reversible potential lies between 20 and 30 kg.-cals. J. A. V. Butler⁷⁴ has developed a similar treatment, differing in some details, and finds $W = 7-27$ kg.-cals. for this reaction. Obviously these calculations will not give accurate values of W , but they show that this stage of the reaction may well have an energy of activation of the same order as that observed.

It is easily shown* that a cathodic overpotential will reduce W by αVF , where $0 < \alpha < 1$. The exact value of α depends on the relative slopes of the two Morse curves at the point of intersection, and is likely to be of the order of 0.5. At the same time the energy

⁷⁵ *Nature*, 1934, **133**, 292.

⁷⁶ See N. K. Adam, "Physics and Chemistry of Surfaces," 2nd edition, Oxford, 1938, p. 332.

⁷⁷ *Rec. Trav. chim.*, 1923, **42**, 718; T. M. Lowry, *Chem. and Ind.*, 1923, **42**, 43.

⁷⁸ *Chem. Reviews*, 1928, **5**, 321.

* See, e.g., Horiuti and Polanyi.⁷³

of activation of the reverse process—the transition of a proton from an adsorption position on the surface to a water molecule—is increased by $(1 - \alpha)VF$. These changes will alter the forward and the reverse reaction velocities by factors of $e^{\alpha VF/RT}$ and $e^{-(1-\alpha)VF/RT}$ respectively. As the net rate of deposition, i , is the difference of these two velocities, this leads to $i = i_0 (e^{VF/2RT} - e^{-VF/2RT})$ if $\alpha = 0.5$ ⁷⁰.

At high overpotentials this relation reduces to the usual logarithmic equation of the type (6) or (1). It also suggests that there will be a similar logarithmic relation on the anodic side of the reversible potential. This theory indicates that the energy of activation, W , will be lowest on metals with a large heat of adsorption for hydrogen,⁷³ in general agreement with experiment.⁴⁸

The effect of changes of p_H on the overpotential due to a mechanism of this type has been investigated by Frumkin.²⁵ Adopting O. Stern's theory⁷⁹ of the double layer, he assumes that the rate of the reaction depends directly on the concentration of hydrogen ions adsorbed at the interface and on the potential difference across the non-diffuse, "Helmholtz", part of the double layer. The ratio of the concentration of adsorbed ions at the surface to the bulk concentration in turn depends on the diffuse potential, ζ . The ζ potential and the Helmholtz potential together make up the total potential difference across the interface. Using the expressions developed by Stern, Frumkin shows that the overpotential should be independent of p_H in solutions of pure acids, but should become 0.058 volt more negative for a unit increase of p_H in solutions containing an excess of a foreign electrolyte.

The three processes considered above are summarised schematically in Fig. 10.

It will be seen that stage I must take place in all cases; it may be followed either by IIa or by IIb. The reaction will in fact proceed by the *faster* of the two alternative processes, IIa and IIb. As indicated above, the reaction velocity and the overpotential are controlled by the *slower* of the two stages I and II (cf. G. Okamoto⁶⁷).

It is now generally accepted that no one mechanism can explain all the features of hydrogen overpotential on different metals.⁸⁰ In particular, the behaviour of platinum and similar metals is very different from that of mercury. This division into two classes is brought out very clearly by measurements of the isotopic separation factor^{33, 34} [about 7 for platinum, nickel, silver, etc.; about 3 for mercury, tin, lead (in acid)], and of its temperature coefficient.³⁴ It is interesting to note that this classification includes silver and nickel in the platinum rather than the mercury group.

⁷⁰ *Z. Elektrochem.*, 1924, **30**, 508.

⁸⁰ *Ann. Reports*, 1937, **34**, 108.

Evidence from several sources indicates that hydrogen is not appreciably adsorbed on mercury surfaces,^{69, 81} and the simple

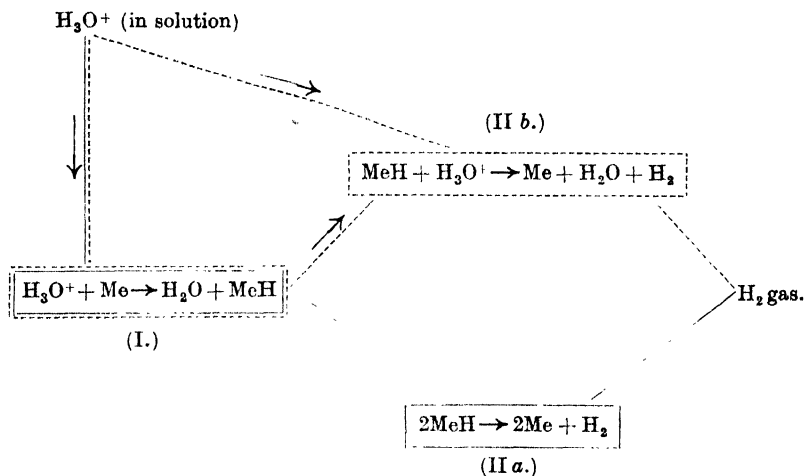


Fig. 10.

theory sketched on p. 103 should therefore apply to the "Tafel" mechanism (IIa). As this leads to a value of α which is 4 times too large, stage IIa cannot determine the reaction rate on mercury. On similar grounds it has been considered that the electrochemical mechanism IIb does not control the velocity on mercury, since this would also be expected to give a value of α greater than unity. Frumkin therefore supposes⁸¹ that the process is in this case controlled by the neutralisation stage. On the other hand, Horiuti and his co-workers^{68, 69} arrive at the value $\alpha = 0.6$ for mercury, after a detailed investigation of this mechanism. They also calculate the actual *C.D.* at a specified overpotential, and the isotopic separation factor, and show that these are in agreement with experiment. In addition, their theory predicts a low value for the temperature coefficient of the separation factor, although not as low as that actually observed. Further support for this mechanism comes from the observation of the difference between the separation factor, and the ratio of deposition rates at a specified potential in pure light and heavy waters¹⁷ (see p. 98). It has been pointed out that this is readily explicable if *two* atoms take part in the rate-determining process.³⁴

On platinum, nickel, and similar metals the situation is radically different, since the evidence indicates that these metals are covered with a fairly complete layer of adsorbed hydrogen on the cathodic

⁸¹ *Acta Physicochim. U.R.S.S.*, 1937, **7**, 475.

side of the reversible potential.⁸² Low values of α are therefore explicable by any of the three mechanisms, I, IIa, IIb. The value of the separation factor shows, however, that the slow step on these metals is generally different from that on mercury. In the case of nickel the theoretical treatment of Horiuti and his co-workers^{66, 69} suggests strongly that IIa is the rate-controlling process. They calculate the values of the isotopic separation factors and of the energy of activation, which agree with experiment, and show that this mechanism provides a good semi-quantitative explanation of the anodic electro-solution of hydrogen on nickel in alkaline solutions. Some other characteristics (*e.g.*, high and variable values of α ,^{15, 21, 39} similarity of kinetics in alkaline and acid solutions^{37, 38, 46}) of the overpotential on metals of this class support the above view (see table). On the other hand, it is difficult to explain the observations of Volmer and Wick³⁶ on the anodic reaction, on this basis; it is also to be expected that when the surface becomes saturated with hydrogen atoms, no further increase of the deposition rate can occur^{33, 74} ($\alpha = 0$), and the potential should rise until some alternative process sets in. It is difficult to disentangle such potential increases at high *C.D.*'s from resistive effects, and they may occur in some cases. But there is no such break shown in the results of Kabanov,¹⁹ who has measured the overpotential on platinum up to 100 amps./sq. cm., or in the work summarised in the table. It thus seems most probable that more than one mechanism may be responsible for the overpotential on these metals according to the state of the surface, the potential, etc.

Some further information about the mechanism of overpotential can be obtained from experiments on other related processes. These include (a) isotopic exchange between gas and solution at an electrode,^{83, 84} (b) the ortho-para-hydrogen interconversion on electrode surfaces,⁸³ (c) the diffusion of hydrogen into and through the electrode metal.^{86, 87, 88}

Although a certain amount of work on these lines has already been carried out, the results cannot yet be clearly interpreted. There is, however, evidence for the following statements. (i) The interchange reaction on platinum has practically the same velocity as the ortho-para conversion.^{83, 85} As the latter depends on the splitting of molecules into atoms, it would appear that the same process controls the transference of a hydrogen particle from the solution to gas phase, or *vice versa*, on the electrodes used. (ii) Ex-

⁸² See refs. (49)–(52).

⁸³ D. D. Eley and M. Polanyi, *Trans. Faraday Soc.*, 1936, **32**, 1388.

⁸⁴ M. Calvin, *ibid.*, p. 1428; M. Calvin and H. Dyas, *ibid.*, 1937, **33**, 1492.

⁸⁶ J. A. V. Butler, *Z. Elektrochem.*, 1938, **44**, 55.

periments on diffusion of cathodically liberated hydrogen through iron and palladium^{86, 87, 88} suggest that the activity of hydrogen atoms on the surface may reach very high values. It seems that the recombination is again a slow process, particularly on poisoned electrodes.⁸⁷ In this connexion it may be mentioned that C. A. Knorr and E. Schwartz⁶⁵ found a close relation between the rate of solution of gaseous hydrogen in palladium wires, and the value of i_0 for the electrodeposition of hydrogen on the same wires (saturated with hydrogen).

The subject is clearly very complicated, and it is difficult to come to a final conclusion. More precise experimental work is required, and it is especially important to co-ordinate overpotential measurements with the other phenomena which are associated with the electrode reactions.

Concentration Overpotential.—Although concentration overpotential plays an important part in a great many electrode reactions,^{3, 4, 6} there are comparatively few in which it is known to be the only cause of irreversibility. This is the case in the deposition of mercury or of iodine from aqueous solutions.⁵⁸ Concentration overpotential is also very important in the deposition of chlorine and bromine,^{56, 89} but it has been shown that a small activation overpotential also occurs in the case of chlorine.⁵⁸ This activation overpotential becomes relatively more important if the concentration overpotential is diminished by vigorously stirring the solution.

Several investigations of overpotential in fused salts have been made recently,^{4, 90, 91} and the existence of concentration overpotential has been established in some cases.^{4, 90} It seems likely that activation overpotential is generally negligible at temperatures such as those used in this work. This is exemplified by a recent investigation of the electrodeposition of oxygen from fused sodium hydroxide.⁴ In contrast to the state of affairs in aqueous solutions,

⁸⁶ A. Coehn and W. Specht, *Z. Physik*, 1930, **62**, 1; C. G. Fink, H. C. Urey, and D. B. Lake, *J. Chem. Physics*, 1934, **2**, 105, 301; T. N. Morris, *J. Soc. Chem. Ind.*, 1935, **54**, 7 r.

⁸⁷ A. H. W. Aten and M. Zieren, *Rec. Trav. chim.*, 1929, **48**, 944; 1930, **49**, 641; P. C. Blokker, *ibid.*, 1936, **55**, 979; P. C. Blokker and A. H. W. Aten, *ibid.*, 1931, **50**, 943.

⁸⁸ L. Sabinina and L. Polonskaja, *J. Phys. Chem. Russia*, 1935, **6**, 107; S. Makareva, *ibid.*, 1934, **5**, 1380 (see A., 1937, 33, 24).

⁸⁹ R. Luther and F. J. Brislee, *Z. physikal. Chem.*, 1903, **45**, 216; G. Pfeiderer, *ibid.*, 1909, **68**, 49; E. Newbery, *J.*, 1921, **119**, 477.

⁹⁰ S. Karpatshev and W. Patzug, *Z. physikal. Chem.*, 1935, **A**, **173**, 383; S. Karpatshev and O. Poltaratskaja, *Acta Physicochim. U.R.S.S.*, 1937, **6**, 275.

⁹¹ S. Karpatshev and S. Rempel, *J. Phys. Chem. Russia*, 1936, **8**, 134; S. Karpatshev and O. Poltaratskaja, *J. Physical Chem.*, 1936 **40**, 763.

it is found that activation overpotential is negligibly small even at high *C.D.*'s. The irreversibility observed, which is considerable, is a concentration overpotential due to the liberation of *water* at the anode.

In connexion with the electrolysis of fused salts, it has been pointed out⁹² that many metals, when deposited from such electrolytes, go into solution to some extent in the melt. This affects the apparent current efficiency and also the electrode potential, until the melt becomes saturated.

The dependence of the concentration at an electrode on *time* was investigated theoretically in an important paper by H. J. S. Sand,⁹³ and has also been considered by Rosebrugh and Lash Miller.⁵ The expressions derived can be adapted to the calculation of the growth of concentration overpotential from the moment that current is switched on.⁴

Lord Rothschild⁹⁴ has shown that the potential of a calomel electrode may change when a current is passed through it. This change, which is of considerable practical importance, is evidently due to concentration changes in the electrolyte near the electrode surface.

Dropping Electrodes.—Numerous papers on the dropping-mercury electrode by J. Heyrovský and his collaborators have been published during the last few years. Useful summaries have been given by him⁹⁵ and by O. Gatty and E. C. R. Spooner.⁹⁶

The Double Layer and Electro-capillarity.—The potential differences which generally exist at an interface must originate in a separation of electric charges of opposite signs. H. von Helmholtz⁹⁷ supposed that this charge was confined to a monolayer, whereas Gouy⁹⁸ and Chapman⁹⁸ considered that there was a region of diffuse charge in the solution. Neither view is entirely satisfactory by itself, but the synthesis of the two views accomplished by Stern⁷⁹ seems to give at least a qualitatively correct picture.

Any change of electrode potential must involve a change in the charge of the double layer as a whole (both the diffuse and the "Helmholtz" portion). This can occur either (*a*) by a direct

⁹² P. Drossbach, *Z. Elektrochem.*, 1938, **44**, 288 (and earlier work).

⁹³ *Phil. Mag.*, 1901, **1**, 45.

⁹⁴ *Proc. Roy. Soc.*, 1938, *B*, **125**, 283.

⁹⁵ *Act. sci. ind.*, **90**, Paris, 1934; J. Heyrovský and J. Klumpar, *Coll. Czech. Chem. Comm.*, 1938, **10**, 153 (bibliography).

⁹⁶ "Electrode Potential Behaviour of Corroding Metals in Aqueous Solutions," Oxford, 1938 (Appendix III).

⁹⁷ "Gesammt. Abh.," 1879, **1**, 925.

⁹⁸ G. Gouy, *Ann. Chim. Phys.*, 1903, [vii], **29**, 145 (and see Frumkin,¹¹ for further references); D. L. Chapman, *Phil. Mag.*, 1913, **25**, 475.

transition of ions across the metal-solution interface or (b) through an external circuit. In the case of mercury in contact with solutions of acids or simple salts there is a considerable range of potential in which both the dissolution of mercury ions and the deposition of hydrogen are extremely slow. At such an electrode, which is "completely polarisable,"⁹⁹ all the increase in the charge of the double layer must pass through an external circuit and can be measured. The ratio of increment of charge to increment of potential is the capacity of the double layer, which may be regarded as an electrostatic condenser. The capacity can be measured in the manner indicated either by observations of the rate of increase of potential at a steady small current,^{15, 100, 101} or by the use of alternating current.^{102, 103} Alternatively, the charge on a mercury surface can be measured at different potentials by a dropping electrode.^{104, 105, 106}

It is also possible to calculate the capacity from electro-capillary data. According to the theory originally developed by G. Lippmann¹⁰⁷ and Helmholtz,⁹⁷ $C = d^2\sigma/dV^2$, where C is the capacity, σ the surface tension, and V the potential across the interface. In recent years a rigid thermodynamical theory of electro-capillarity has been developed,^{99, 108} and the above relation has been deduced without resorting to the somewhat crude physical picture required by earlier derivations. It may also be noticed that the total potential V across the interface between two different media cannot be measured, and in this sense is without physical meaning.¹⁰⁹ For the present purpose, however, it is only changes in V which are of importance.

The very extensive series of experiments on electro-capillarity carried out by Gouy⁹⁸ show that the double layer capacity is about 20 $\mu\text{F.}$ over a considerable range of potential. Outside this range

⁹⁹ O. Koenig, *J. Physical Chem.*, 1934, **38**, 111.

¹⁰⁰ F. Krüger, *Z. physikal. Chem.*, 1903, **45**, 1; H. Brandes, *ibid.*, 1929, **A**, 142, 97.

¹⁰¹ T. Erdey-Grúz and G. Kromrey, *ibid.*, 1931, **A**, 157, 213.

¹⁰² M. Proskurnin and A. Frumkin, *Trans. Faraday Soc.*, 1935, **31**, 112; and see Gatty and Spooner, *op. cit.*, p. 485.

¹⁰³ T. Borissova and M. Proskurnin, *Acta Physicochim. U.R.S.S.*, 1936, **4**, 819.

¹⁰⁴ A. Frumkin, *Z. physikal. Chem.*, 1923, **A**, 103, 43, 55.

¹⁰⁵ J. St. L. Philpot, *Phil. Mag.*, 1932, **13**, 775.

¹⁰⁶ D. Ilkovic, *Coll. Czech. Chem. Comm.*, 1936, **8**, 170.

¹⁰⁷ *Ann. Chim. Phys.*, 1875, **5**, 494.

¹⁰⁸ S. R. Craxford, O. Gatty, and others, *Phil. Mag.*, 1933, **14**, 849; 1934, **17**, 54; 1935, **19**, 965; 1936, **22**, 359.

¹⁰⁹ E. A. Guggenheim, *J. Physical Chem.*, 1929, **33**, 842; 1930, **34**, 1540; "Modern Thermodynamics," 1933, Chap. 10.

the capacity increases somewhat, and there is also evidence of an intermediate maximum at about -0.5 volt on the calomel scale. This corresponds to the electro-capillary maximum. These results are obtained in the majority of simple salts, but in solutions of "capillary active" substances, the situation is less simple, and different values of the capacity are observed.¹¹⁰ Experiments with dropping electrodes¹⁰⁴⁻¹⁰⁶ give similar results. On the cathodic side of the capillary maximum the capacity is of the order $20 \mu\text{F.}$, and practically independent of the nature of the ions in the solution. On the anodic side higher values are observed,¹⁰⁵ and these depend to some extent on the nature and particularly the polarisability of the anion present.

Until recently, all attempts to measure the capacity by the direct method gave lower values than the other two methods,^{15, 101} although it was shown¹⁰¹ that the variation of the capacity with the potential was closely parallel to that observed by Gouy. This discrepancy has now been cleared up. Proskurnin and Frumkin¹⁰² measured the capacity at a freshly formed mercury surface by an alternating-current method, and found values almost identical with those observed by Gouy. If the surface were contaminated, however, a value about 4 times lower was observed. Bowden and Grew,²⁰ working at very low $C.D.$'s, find that if a mercury surface is protected from contamination by being completely enclosed in glass, it has capacity of $20 \mu\text{F./sq. cm}$

The direct method of measuring capacities can be applied to nearly all metals. With liquid gallium and Wood's metal, Bowden and O'Connor¹⁴ found a value identical with that for mercury. More recently, electro-capillary experiments have been carried out with gallium,¹¹¹ and these lead to a capacity of about $20 \mu\text{F./sq. cm.}$ In the case of solid metals the capacity depends upon the real surface area and is always greater than that for mercury.¹⁵

Direct surface-tension experiments cannot be carried out on solid metals; but the angle of contact of bubbles or oil drops on the surface depends on the metal-solution surface tension,¹¹² and the variation of this with potential can be calculated from observations of the contact angle.¹¹³ In this way an "electro-capillary" curve for platinum has been obtained. This work has been summarised by Frumkin.¹¹

¹¹⁰ A. Frumkin, *Z. Physik*, 1926, **35**, 792.

¹¹¹ A. Murtazajew and A. Gorodetzka, *Acta Physicochim. U.R.S.S.*, 1936, **4**, 75; A. Frumkin, *Physikal. Z. Sovietunion*, 1933, **4**, 239.

¹¹² G. Möller, *Ann. Physik*, 1908, [iv], **27**, 665; *Z. physikal. Chem.*, 1908, **65**, 226.

¹¹³ A. Frumkin, B. Kabanov, and others, *Z. physikal. Chem.*, 1933, **4**, 165, 433; *Physikal. Z. Sovietunion*, 1932, **1**, 255; 1934, **5**, 418.

A good account of electro-capillary phenomena in general, and of overpotential, has been given recently by N. K. Adam.¹¹⁴ An interesting experimental and theoretical account of the electrode potentials of corroding metals has been published by Gatty and Spooner.⁹⁶ Evidence is brought forward for the existence of inhibitive hydride films on iron and several other metals. The electrochemical basis of corrosion in general has been fully treated in Evans's recent book¹³ on that subject.

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¹¹⁴ *Op. cit.*; see also A. Frumkin, *Ergebn. exakt. Naturwiss.*, 1928, 7, 235; Gatty and Spooner, *op. cit.*, Appendix V.

INORGANIC CHEMISTRY.

1. INTRODUCTION.

DURING the past year work in Inorganic Chemistry has continued along well-defined lines, and progress has been more in the nature of elucidation of older problems rather than of a fundamental type. It is not to be inferred, however, that work in this branch has lacked interest. The use of more exact or more powerful methods has led to a clearer insight into the course of reactions and into the structure of inorganic substances, and it is in these directions that advances have been made.

Although an enormous number of observations on the ozone content of the atmosphere have been carried out since the time of C. F. Schönbein (1845) doubt of the accuracy of the data (or even of its presence) has always existed owing to the lack of a sufficiently delicate specific reagent for this compound.

F. A. Paneth and J. L. Edgar ¹ by first concentrating the more volatile products in a known volume of air by condensation, followed by separation by fractional distillation, have conclusively shown that ozone is present in the air and have estimated its concentration in London and at Kew. The ozone purified in this manner from other oxidising agents, especially oxides of nitrogen, can be determined by the potassium iodide-starch method or spectroscopically. These observers find that the average concentration of ozone in London air is 1.1×10^{-6} vol. %.

By means of a balloon and a self-registering ultra-violet spectrograph, efforts have been made to determine the vertical distribution of ozone in the atmosphere. V. H. Regener's ² measurements seem to indicate that the ozone concentration decreases from a height of 14 km. to a sharp minimum between 5 and 12 km. Although reasons for this concentration change have been put forward, it is perhaps unsafe to discuss them, for, owing to the complications in the method due to absorption of light by dust particles and Rayleigh scattering, the results are not free from criticism. It is to be hoped that Paneth, as indicated in his letter, will extend his observations to higher altitudes.

By measurement of the absorption in a limited region of the

¹ *Nature*, 1938, **142**, 112.

² *Naturwiss.*, 1938, **26**, 155; *Z. Physik*, 1938, **109**, 642.

spectrum, G. Dejardin, A. Arnulf, and D. Cavassilas³ have computed that the thickness of the ozone layer, reduced to normal temperature and pressure, is 0.290 cm. $\pm 5\%$. The difficulties of this method, however, apply equally here, and the estimated accuracy is probably unreal.

In the atmosphere, the argon : neon ratio is of the order 520 : 1, but in celestial sources neon is much more abundant. H. A. Russell and D. N. Menzel⁴ explained this on the supposition that the atmosphere lost most of its neon in earlier times when the earth temperature was very high. Support for this view has been brought forward by (Lord) Rayleigh⁵ from an examination of the neon and argon content of granite. Four samples from different sources were examined, and it was found that the quantities per g. of granite were of the order 10^{-6} c.c. of neon and 4×10^{-5} c.c. of argon, i.e., a ratio of about 40 : 1.

The realisation that fluorine could be readily prepared in apparatus other than platinum* has led to a more extended investigation of this element, and most of its physical properties have now been determined, e.g., viscosity, surface tension, molecular heat of fusion, entropy,⁶ and electrode potential. L. O. Brockway⁷ has measured the internuclear distance in the molecule by electron diffraction, obtaining a value of 1.45 Å., and hence for the covalent radius of the atom a value of 0.73 Å. The distance calculated from other fluorides, e.g., methyl fluoride, is 0.64 Å., so that in the fluorine molecule the distance is about 14% greater than the value expected for a normal covalent single bond. A Raman spectrum could not be detected.⁸

Purification from oxygen,⁹ a common impurity, can be brought about by the fact that the latter element is more readily adsorbed by charcoal at low temperatures than fluorine, five adsorptions at -180° being sufficient to decrease the oxygen content from 3.5% to 0.4%.

In the solid form fluorine reacts normally very vigorously with hydrogen except in capillaries or in old glass vessels, where an explosion could not be induced at room temperatures even under irradiation. This inhibition is thought to be due to silicon tetrafluoride acting as a negative catalyst.¹⁰

³ *Compt. rend.*, 1937, **205**, 809. ⁴ *Proc. Nat. Acad. Sci.*, 1933, **19**, 997.

⁵ *Nature*, 1938, **141**, 410.

⁶ E. Kanda, *Bull. Chem. Soc. Japan*, 1937, **12**, 463, 469, 511.

⁷ *J. Amer. Chem. Soc.*, 1938, **60**, 1348.

⁸ C. S. Garner and D. M. Yost, *ibid.*, 1937, **59**, 2738.

⁹ E. Kanda, *Bull. Chem. Soc. Japan*, 1937, **12**, 455.

¹⁰ *Idem, ibid.*, p. 521.

* For the latest type of fluorine generator, see A. L. Henne, *J. Amer. Chem. Soc.*, 1938, **60**, 6096.

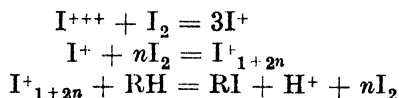
The white product formed when fluorine acts on tellurium has been shown to be the tetrafluoride¹¹ and not the difluoride as formerly supposed.

As mentioned in last year's Reports,¹² the decomposition of bromine dioxide takes place in stages. The brown product formed has since been shown to be Br_2O , identical with that obtained by W. Brenschede and H. J. Schumacher¹³ by the action of bromine on specially active mercuric oxide.

The composition of iodous sulphate has been finally settled by J. I. O. Masson and C. Argument,¹⁴ who find that the product formed in concentrated sulphuric acid is the anhydrous salt $\text{I}_2\text{O}_3\cdot\text{SO}_3$. This sulphate is prepared by acting on a mixture of iodine pentoxide and iodine with concentrated sulphuric acid. If the acid concentration is reduced to that of $\text{H}_2\text{SO}_4\cdot\text{H}_2\text{O}$ decomposition into the initial products takes place, and in fuming sulphuric acid the compound undergoes transition into a white crystalline sulphate $\text{I}_2\text{O}_3\cdot 4\text{SO}_3\cdot x\text{H}_2\text{O}$. Dilution of the fuming acid leads first to the regeneration of iodine and iodine pentoxide, which then react with the re-formation of $\text{I}_2\text{O}_3\cdot\text{SO}_3$. This fact has induced the authors to put forward the view that in passing from the concentrated to the fuming acid, a transition of the tervalent iodine takes place and that in the fuming acid it is present in the form of a complex, possibly a negative one, whilst in the concentrated acid the bare ion I^{+++} is present.

Iodine is soluble in the acid solution of the yellow sulphate, giving a deep brown colour, the concentration of the iodine taken up per molecule of I_2O_3 present varying from 3.44 I_2 to 11.07 I_2 as the acid strength changes from $\text{H}_2\text{SO}_4\cdot\text{H}_2\text{O}$ to nearly H_2SO_4 . From the reactions of these solutions with organic molecules, *e.g.*, chlorobenzene, which result in the formation of iodo- and not iodonium compounds, and from the fact that if the initial "oxide" solute is expressed as I_xO then exactly I_2O is consumed and the remaining $(x - 2)$ atoms of iodine are precipitated as element, it is concluded that the iodine is present in the univalent form.

These results are expressed by equations thus :



The view that the iodine atoms were present as iodine of

¹¹ R. Whytlaw-Gray, T. H. Henry, and G. A. R. Hartley, *Nature*, 1938, **142**, 952.

¹² *Ann. Reports*, 1937, **34**, 139.

¹³ *Ibid.*, p. 138.

¹⁴ *J.*, 1938, 1702.

solvation¹⁵ or taken up as a micelle was rejected on the grounds that it would necessitate a very complicated and artificial mechanism for aromatic iodinations. It is interesting to note that if the authors' views are accepted we have a parallel between the positive ions of univalent iodine I^+ , I_3^+ , I_5^+ , etc., and the negative ions I^- , I_3^- , I_5^- of the iodides and polyiodides.

Further attempts to demonstrate the polar nature of iodine monochloride have been carried out by C. Sardonnini and N. Borghello¹⁶ by the electrolysis of this substance in acetic acid and in nitrobenzene. The cathode and the anode chamber were separated by glass diaphragms, and platinum electrodes were used. In acetic acid, although the concentration of both halogens increased at the anode, the ratio I to Cl decreased, and the results agreed with the view that the solution contains a small amount of I^+ and ICl_2^- ions, the latter having a much higher migration velocity.

Reactions between iodine monochloride and a number of salts have been investigated.¹⁷ Briefly, the results may be summarised by stating that in some cases chlorides are formed, in others iodides, and some give addition compounds. Thus ammonium, potassium, and rubidium chlorides (but not those of lithium and sodium) form addition compounds of the type MCl, ICl , as do the acetates of the heavy metals lead, copper, and cadmium: $[M_2(OAc)_2]I, Cl$. The nitrates and sulphates of sodium and potassium and a number of cyanides yield chlorides, but the sulphides of cadmium, lead, zinc, and silver are converted into iodides. Cyanates and thiocyanates give chlorides and $I(CON)_3$ and $I(CNS)_3$ respectively.

E. Zintl and W. Morawietz¹⁸ have attempted to classify oxides according to the polarisability, (charge on ion)/(radius of ion), of the positive ion. Those which form glass-like oxides all have values of e/r between 7 and 15. Oxides having values of this quotient greater than 15 constitute the volatile oxides with molecular lattices, and those with $e/r < 7$ are the salt-like oxides with co-ordination lattices as their structure. In the case of the latter, the authors attempted to determine the co-ordination number of the ion by the preparation of ortho-salts. This possibility rests on the assumption that when a sufficient amount of a strongly basic oxide is present all oxygen bonds of the acid oxide are broken down and that the whole of the oxygen present may be looked upon as co-ordinated to the acid-forming element.¹⁹

¹⁵ Cf. A. C. D. Rivett and J. Packer, *J.*, 1927, 1342.

¹⁶ *Atti R. Accad. Lincei*, 1937, [vi], 25, 46.

¹⁷ J. Cornog, H. W. Horrabin, and R. A. Karges, *J. Amer. Chem. Soc.*, 1938, 60, 429.

¹⁸ *Z. anorg. Chem.*, 1938, 236—237, 372.

¹⁹ In the paper the grounds for this assumption are discussed.

The ortho-salts were made by heating decreasing amounts of sodium oxide with the acid oxide or a salt in a vacuum and then subjecting the product to X-ray examination. When the spectrum of Na_2O was no longer visible it was inferred that the maximum combining power of base to acidic oxide had been attained, and the composition of the product was determined at that stage. The results are given in the subjoined table, the number below the central element indicating its co-ordinating value.

NaOH 1	Na_4BeO_3 3	Na_3BO_3 3	Na_2CO_3 3	$\text{Na}_3\text{N}^{\text{VO}}\text{O}_4$ 4	$\text{Na}_2\text{SO}_4, \frac{1}{2}\text{Na}_2\text{O}$ 4	NaClO_4 4
Na_3AgO_2 2		Na_5AlO_4 4	Na_4SiO_4	$\text{Na}_3\text{N}^{\text{III}}\text{O}_3$ 3	$\text{Na}_2\text{SeO}_4, \frac{1}{2}\text{Na}_2\text{O}$ 4	
			$\text{Na}_4\text{Sn}_2\text{O}_4$			Na_5IO_6 6
			$\text{Na}_4\text{PbO}_4, \text{Na}_2\text{O}$ 4	Na_3PO_4 4	Na_6TeO_6 6	

The formation of ortho-salts of nitric and nitrous acids is of interest. Sodium hydroxide showed no tendency to combine with sodium oxide: the ion $[\text{OHO}]^{---}$ analogous to the bifluoride ion FHF^- seems incapable of existence. It should be noted that in the preparation of these ortho-salts, sodium oxide must be used. Energy considerations prevent in certain cases the formation when the hydroxide or carbonate is substituted. Moreover, the value of the co-ordination number derived in this way is not always in agreement with that obtained from consideration of ionic size.

Confirmation of the existence of the oxide of lead, Pb_7O_{11} , reported last year,²⁰ could not be obtained by A. Baroni,²¹ who, in the decomposition of lead dioxide or by the action of oxygen on the monoxide under pressure, could only detect the well-known species Pb_2O_3 and Pb_3O_4 . His X-ray and magnetic work further tends to confirm the view that Pb_2O does not exist,²² but that it is a mixture of the metal and tetragonal PbO .

Working under different conditions, i.e., by heating the dioxide with aqueous sodium hydroxide in a pressure bomb, G. L. Clark, N. C. Schieltz, and T. T. Quirke²³ found, in addition to crystals of Pb_2O_3 and Pb_3O_4 , large single crystals of Pb_5O_8 , the three oxides being formed at temperatures of 260—275°, 355—375°, and 295—310° respectively under their conditions.

Five papers²⁴ have been published on the higher oxides of nickel.

²⁰ *Ann. Reports*, 1937, **34**, 150. ²¹ A. Baroni, *Gazzetta*, 1938, **68**, 387.

²² Cf. *Ann. Reports*, 1937, **34**, 150.

²³ *J. Amer. Chem. Soc.*, 1937, **59**, 2305.

²⁴ F. François and (Mlle.) M. L. Delwaille, *Compt. rend.*, 1937, **204**, 1042; 205, 282; B. A. Petrov and B. Ormont, *J. Gen. Chem. Russia*, 1938, **8**, 563; D. P. Bogatzki, *ibid.*, 1937, **7**, 1397; J. H. Krepelka and M. Blabolil, *Coll. Czech. Chem. Comm.*, 1937, **9**, 497.

Possibly the best way of looking upon these oxides, whether made from the ignition of nickel nitrate or by the action of oxidising agents on nickel salt solutions, is as a series of solid solutions of NiO and NiO₂. According to Bogatzki, the intermediate oxides differ from NiO only in their larger space lattice constant. The possibility of replacing bivalent nickel in the nickel oxide lattice by higher-valent nickel giving rise to non-stoicheiometric or "Berthollide" oxides, must be borne in mind, and even the fact that Ni₁O₁ itself may actually be non-existent.

A disconcerting result, especially to analytical chemists, is the observations of A. Westgren and K. Dohlström²⁵ that the product formed by heating antimonious acid for 3 hours at 780° was not the tetroxide, Sb₂O₄, but Sb^{III}O(OH),Sb^V₂O₅, a structure apparently confirmed by comparison with the isomorphous compound BiTa₂O₆F. The above procedure is the one commonly recommended for the quantitative determination of antimony as Sb₂O₄ and has been checked by many observers, and to the Reporter it must appear that SbO(OH),Sb₂O₅ is capable of losing water (and oxygen) without change of structure, a feature observed also in CaSO₄· $\frac{1}{2}$ H₂O. It is only when the last traces of water are removed that the lattice breaks down from the face-centred cubic of the hydrated compound to the rhombic form of the tetroxide.

It has long been known that when ammonium dichromate is gently ignited a black solid residue is left, which on stronger heating changes over into a green mass universally assumed to be chromic oxide. K. Fishbeck and H. Spengler,²⁶ who carried out the decomposition in a vacuum at a temperature of 160—250°, concluded that the black product was Cr₂O₃·H₂O. Closer examination by E. H. Harbord and A. King,²⁷ however, reveals the fact that this substance is not homogeneous and that on heating it evolves not only water but nitrous oxide and nitrogen: moreover, strong ignition did not result in the formation of Cr₂O₃, but of an oxide containing more oxygen, possibly a non-stoicheiometric compound.

A still lower oxide of sulphur,²⁸ S₂O, is said to exist in the yellow solution formed when SO is passed into dry carbon tetrachloride. It decomposes rapidly into sulphur and the dioxide, but can be stabilised in this solvent to some extent by the addition of dry hydrogen chloride. The evidence for its existence is based on the observation that on treatment of the carbon tetrachloride solution with sodium hydroxide, equivalent amounts of sodium sulphide and sulphite are formed.

²⁵ *Z. anorg. Chem.*, 1938, **235**, 153; K. Dohlström, *ibid.*, 1938, **236**, 57,

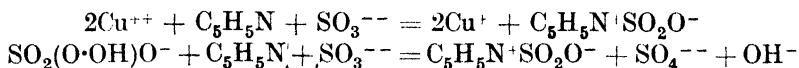
²⁶ *Ibid.*, 1938, **235**, 183.

²⁷ *J.*, 1938, 955,

²⁸ B. S. Rao, *Current Sci.*, 1938, **6**, 386,

By the reduction of dilute hydrochloric acid solutions of rhenium with zinc and with cadmium respectively, the hydrated forms of the two lower oxides $\text{Re}_2\text{O}_3 \cdot 2\text{H}_2\text{O}$ and $\text{ReO}_2 \cdot \text{H}_2\text{O}$ have been isolated.²⁹ Both exist in the form of black powders insoluble in hydrochloric acid or sodium hydroxide, but rapidly attacked by oxidising agents such as nitric acid or bromine water.

P. Baumgarten and H. Erbe³⁰ have made an extended study of the oxidation of sulphite solutions, using substances capable of yielding stable compounds with the unstable intermediates as indicators. All the latter possessed pronounced co-ordinative characteristics and included pyridine, urea, dioxan, glycine, ammonia, boric acid, and alkali fluoride. Three types of sulphite oxidation were distinguished: (1) Cupric salts and Caro's acid, HSO_5 , which with pyridine as indicator gave pyridiniumsulphonic acid in addition to sulphate and dithionate:

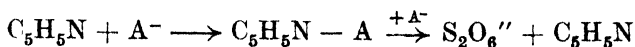


(2) Anodic oxidation and potassium persulphate, which do not yield the above pyridinium salt but in the absence of an indicator give a greater yield of dithionate. (3) Hydrogen peroxide, which gives almost exclusively sulphate.

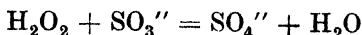
These results are explained on the assumption of the production of ions A and B. Whether the ion is discharged at (a) or (b) depends



on the oxidising agent, (B) being the intermediate when pyridiniumsulphonic acid is produced, whereas (A) is prominent when dithionate is formed. The probable reaction in the latter case is



With hydrogen peroxide the main process is in all probability an immediate transference of oxygen from H_2O_2 to SO_3^{--} , thus:



S. R. Das³¹ has made a study of the sulphur allotropes, and has shown that roll sulphur, flowers of sulphur, milk of sulphur, and the gummy deposits of colloidal sulphur are all S_8 (orthorhombic

²⁹ R. C. Young and J. W. Irvine, *J. Amer. Chem. Soc.*, 1937, **59**, 2648.

³⁰ *Ber.*, 1937, **70**, 2235.

³¹ *Indian J. Physics*, 1938, **12**, 163.

sulphur). Hydrolysis of sulphur monochloride gives a white form, definitely crystalline but different from S_a , into which, however, it is easily converted by heating to 88° . Fresh plastic sulphur is amorphous, giving a diffuse band which coincides with one of the bands of liquid sulphur. No change in the structure of sulphur was observed on cooling to -183° .

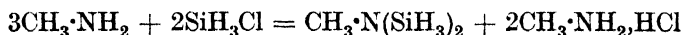
A reinvestigation of Bridgman's observation that white phosphorus was irreversibly converted into a black modification at 12,000 atm. and about 200° has been undertaken by R. B. Jacobs.³² This black form differs from the ordinary black crystalline modification in being amorphous and having a lower density. Prolonged heating of this amorphous powder at 125° yielded a brilliant violet modification of red phosphorus.

Further support for regarding the diammoniate of diborane³³ as being a monoammonium salt,³⁴ $NH_4^+H_3BNH_2BH_2^-$, in which an atom of nitrogen is interposed in the boron chain, has been obtained from a study of B_2H_7N .³⁵ This compound, which has m. p. -66.5° and b. p. 76.2° , is easily prepared by the action of B_2H_6 on $B_2H_6 \cdot 2NH_3$. Acids hydrolyse it, giving 5 mols. of hydrogen, 2 mols. of boric acid and one ammonium ion. It reacts with an

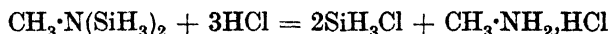
equal volume of trimethylamine, giving a stable white solid which, on heating, gives borine trimethylamine and takes up one molecule of ammonia, forming $B_2H_7N \cdot NH_3$. In liquid ammonia the latter reacts with sodium, forming $NaNH_2 \cdot B_2H_7N$. These reactions are in harmony with the structure (I), which

is supported by the electron-diffraction work of S. H. Bauer,³⁶ who finds a B-N-B skeleton.

Some interesting new derivatives of the silyl radical have been prepared by H. J. Emeléus and N. Miller³⁷ by the interaction of monochlorosilane and amines. For instance, with methylamine the following reaction takes place :



The product, methyldisilylamine, is a liquid, b. p. 325° , hydrolysed by alkali and decomposed by hydrochloric acid :



With trimethylamine a stable, solid, quaternary compound is formed, $N(CH_3)_3 \cdot SiH_3Cl$. This is decomposed by water into trimethyl-

³² *J. Chem. Physics*, 1937, **5**, 945.

³³ Cf. *Ann. Reports*, 1937, **34**, 152.

³⁴ H. I. Schlesinger and A. B. Bury, *J. Amer. Chem. Soc.*, 1938, **60**, 290.

³⁵ H. I. Schlesinger, D. M. Ritter, and A. B. Bury, *ibid.*, p. 2297.

³⁶ *Ibid.*, p. 524.

³⁷ *Nature*, 1938, **142**, 996.

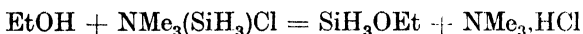
amine hydrochloride and disiloxane, $(\text{SiH}_3)_2\text{O}$, and is hydrolysed by alkali :



This salt has a dissociation pressure of 1 atm. at 91° . This dissociation is not reversible at higher temperatures, owing to the disproportionation of the SiH_3Cl formed :



It is a useful silylating agent, for it reacts with alcohols to form silyl alkyl ethers :



Monochlorosilane and dimethylamine react at room temperature, forming $\text{N}(\text{SiH}_3)\text{Me}_2$. This tends to unite with an excess of the monochlorosilane, giving an unstable quaternary salt. As pointed out by the investigators, there is a decrease in the stability of the quaternary salts as CH_3 is replaced by SiH_3 :

NMe_4Cl	Stable	$\text{NMe}(\text{SiH}_3)_3\text{Cl}$	Not formed
$\text{NMe}_3\text{SiH}_3\text{Cl}$	Moderately stable	$\text{N}(\text{SiH}_3)_4\text{Cl}$	Not formed
$\text{NMe}_2(\text{SiH}_3)_2\text{Cl}$	Unstable		

A new view for the change in colour under varying conditions of cobalt salt solutions has been put forward by J. N. Pearce and L. R. Dawson.³⁸ Of the older ideas, one school ascribed the change of the red solution on the addition of chlorides to the formation of the complex ion CoCl_4^{--} , whereas another concluded that the degree of hydration of the cobalt ion changed : in the red solution it was co-ordinated to six molecules of water, whereas in the blue it was tetra-co-ordinated, a view based on the fact that the colour change was linked with the hydrating power of the added cation. Pearce and Dawson point out that the first of the above theories seems inadequate in that equimolecular concentrations of added chloride do not produce equivalent colour changes. They find from an examination of the spectrum that the absorption band is widened by added salt, the extent of which depends directly on the ionic charge and inversely on the ionic volume of the added cation.

The new view regards the cobalt atom in dilute solution as being strongly hydrated, the sheath of water molecules preventing its close approach to the chlorine ion. Addition of strongly hydrating cations removes this sheath and permits electrostatic attraction to bring the cobalt and chlorine ions closer together. This causes a distortion of the electronic system of the cobalt ion, with change in its absorption spectrum.

³⁸ *J. Chem. Physics*, 1938, **6**, 128.

The rare earths have continued to receive attention. By heating the oxides of lanthanum, cerium, praseodymium, neodymium, samarium, and ytterbium with ammonium iodide at 400° the anhydrous iodides of these elements were prepared, excess of ammonium iodide being removed by vacuum sublimation.³⁹ The products were obtained in the form of green, hygroscopic powders readily soluble in organic solvents such as alcohol or pyridine. On exposure to the air, hydrolysis takes place and basic salts are formed.

G. Beck and W. Nowacki⁴⁰ have shown that the lower fluoride and sulphide of europium can be respectively obtained by reducing the trivalent fluoride in a stream of hydrogen and the sulphate in a current of hydrogen sulphide. It is interesting to note that EuF_2 has the fluorite structure with cell dimensions approximating to those of SrF_2 . Elementary europium has been isolated by the electrolysis of the trichloride in a sodium chloride-potassium chloride eutectic mixture.⁴¹

From observations of the amount of oxygen taken up when praseodymium was heated under pressure in that gas, W. Prandtl and G. Rieder⁴² have demonstrated that praseodymium is quinquevalent in the completely oxidised state, whereas under similar conditions terbium tends to quadrivalency.

Seeking better methods for the separation of the rare earths, W. Prandtl and S. Mohr⁴³ have studied the ferro- and ferri-cyanides and their solubility in water and dilute hydrochloric acid. By the action of alkali ferrocyanide on an acid solution of a rare-earth salt, ferrocyanides of the type $\text{NaMFe(CN)}_6 \cdot n\text{H}_2\text{O}$ are obtained. With ferrocyanic acid, basic salts are formed, e.g., with lanthanum, $\text{LaOH}[\text{LaFe(CN)}_6]_2 \cdot 18\text{H}_2\text{O}$. Ferricyanides give compounds of the general type $\text{MFe(CN)}_6 \cdot n\text{H}_2\text{O}$. These are more soluble than the ferrocyanides.

Isotherms, determined at 25° and 50° for the ternary system, cerium group nitrates-nitric acid-water, show that the solubilities do not decrease in the order of increasing atomic number, but that the solubility of lanthanum nitrate is anomalously low, the order found being $\text{Ce} > \text{Pr} > \text{La} > \text{Nd} > \text{Sm}$. In the solid form the nitrates exist as hexa-, tetra-, and tri-hydrates. Observations by J. Newton Friend and D. A. Hall⁴⁴ in the cases of lanthanum and praseodymium on the loss of water from the characteristic hexahydrates could only confirm the existence of the monohydrate for lanthanum and the dihydrate for praseodymium.

³⁹ W. A. Taebel and B. S. Hopkins, *Z. anorg. Chem.*, 1937, **235**, 62.

⁴⁰ *Naturwiss.*, 1938, **26**, 495. ⁴¹ F. Trombe, *Compt. rend.*, 1938, **206**, 1380.

⁴² *Z. anorg. Chem.*, 1938, **238**, 225.

⁴³ *Ibid.*, 1938, **236**, 243; **237**, 160.

⁴⁴ *J.*, 1938, 1920.

It has been known for some years that when nitrogen dioxide was dried over phosphoric oxide union occurred and a glassy compound was formed. This was looked upon as an addition compound P_2O_5, xNO_2 ,⁴⁵ but E. M. Stoddart⁴⁶ finds that in the interaction oxygen is evolved and that the addition compound is really $P_2O_5, 2NO$:



This observation rules out Smith's evidence that intensive drying inhibited the reaction between nitric oxide and oxygen. H. B. Baker's evidence⁴⁷ is now the only indication that drying can influence this reaction.*

No further definite developments have been made since the last Reports with regard to elements nos. 43, 61, 87, and 93. H. Hulubei's claims⁴⁸ to have observed lines corresponding to the L_α , L_α , L_β , and L_γ of element 87 in the alkali concentrates from pollucite have not been confirmed. The same applies to his observations on the presence of a transuranium element no. 93 in minerals containing uranium and rhenium.⁴⁹ Fermi's contention, however, that transuranium elements resulted from the disintegration of activated uranium has been well substantiated by other workers.⁵⁰ H. Jensen⁵¹ has suggested that stable nuclei of elements No. 43 and 61 may not occur. This suggestion is based on Mattauch's rule, which states that if two isobares differ in nuclear charge by unity, one of them must be unstable. Considering element 61, the adjacent members ${}_{60}Nd$ and ${}_{62}Sm$ have many isotopes. This points to an unstable nucleus for an element of atomic number 61. A similar state of affairs occurs with 43. The existence of long-lived β -active isotopes is also considered unlikely.

Work has continued throughout the year on polynuclear metallic complexes and on co-ordination compounds. These are discussed in separate sections of this Report, as is also the separation of isotopes. Investigations on reactions in solvents other than water also received a good deal of attention, in particular the solvents with high dielectric constants and good ionising properties—ammonia, sulphur dioxide, and hydrogen fluoride. The earlier work on ammonia is well summed up by A. Findlay in the Franklin Memorial Lecture :⁵²

⁴⁵ J. W. Smith, *J.*, 1928, 1886.

⁴⁶ *J.*, 1938, 1459.

⁴⁷ *J.*, 1894, 65, 611.

⁴⁸ *Compt. rend.*, 1936, 202, 1927; 1927, 205, 854.

⁴⁹ H. Hulubei and (Mlle.) Y. Couchois, *ibid.*, 1938, 207, 333.

⁵⁰ For a very full account of work on the transuranium elements, see L. L. Quill, *Chem. Reviews*, 1938, 23, 87.

⁵¹ *Naturwiss.*, 1938, 23, 381.

⁵² *J.*, 1938, 583.

* See, however, in this connection E. M. Stoddart, *J.*, 1939, 5.

other solvents such as the alcohols, alkyl halides, acetone, nitrobenzene, and benzene have been used, particularly by V. A. Plotnikov and his co-workers.⁵³

H. T.

2. ATOMIC WEIGHTS.

1936—1938.

In view of the rapid extension of the study of nuclear transformations and their accompanying energy changes, as well as the marked developments in mass spectrography, it is not surprising that purely physical evidence is becoming of increasing importance in this field of chemistry.

Apart from the comparatively large errors in certain atomic weight values indicated by earlier work on mass spectra and usually corrected by chemical revision, data are now available for the examination of smaller differences, and in some cases atomic weight values have been revised solely on the strength of physical evidence. This is the case for the new values $H = 1.0081$, $He = 4.003$, and $Os = 190.2$ in the Eighth Report ¹ of the Committee on Atomic Weights of the International Union. It is now impossible adequately to review the progress in atomic weight research without reference to the new physical material now available. Development has extended mainly in two directions: (1) the measurement of the relative masses of atoms (isotopic weights) either with improved mass spectrographs or by means of nuclear reaction energies, (2) the determination of the relative proportions of the isotopes in complex elements (abundance ratios). Notable progress in both directions has been made during the last two years. F. W. Aston ² has measured by the doublet method with his second-order focusing mass spectrograph the masses of 21 isotopes ranging from hydrogen to mercury with an accuracy approaching 1 part in 10^5 , and just recently he has examined five more, making available the packing fractions and isotopic weights of 24 species determined to a higher order of accuracy. Similar work has been published by K. T. Bainbridge and E. B. Jordan ³ for a number of the lighter elements, *viz.*, hydrogen, deuterium, carbon, helium, beryllium, boron, neon, and argon, an instrument of specially high resolution again being used, whilst A. J. Dempster ⁴ has published work on the heavier elements.

Primarily, the new data are of great importance in nuclear physics,

⁵³ For summary, see *Mem. Inst. Chem. Ukrain. Acad. Sci.*, 1937, **4**, No. 3.
 ¹ *J.*, 1938, 1101.

² *Proc. Roy. Soc.*, 1937, **A**, **163**, 391; *Nature*, 1938, **141**, 1096.

³ *Physical Rev.*, 1936, **49**, 883; 1937, **51**, 384. ⁴ *Ibid.*, 1938, **53**, 64.

for they furnish an independent check on energy changes,⁵ but they also afford the chemist more accurate values for the packing fractions which, taken in conjunction with the abundance ratios, enable more reliable estimates of the atomic weights of a number of elements to be made. It is interesting to note that the values for the isotopic weights from nuclear reactions and from mass spectrography show a remarkable concordance. M. S. Livingston and H. A. Bethe⁶ have critically examined the data available up to 1937 and have published what they judge to be the most accurate values for the isotopic weights from ^1H to ^{40}A .

A striking contribution to the measurement of abundance ratios has been made by A. O. Nier. Using a mass spectrograph specially designed for this purpose, he determines the relative proportions of the isotopes in complex elements by an electrometric method instead of by photometry of the lines on a photographic plate. He has examined A,^{7,9} K, Rb, Zn, Cd,⁷ Hg, ^{8,10} Xe, Kr, Be,⁸ Ca, Ti, S,⁹ Pb,¹¹ Sr, Ba, Tl¹⁰ and Os,¹⁵ as well as I, As, Cs,⁸ Bi.¹⁰ No new isotopes have been detected in the last group, which are single to a high degree. A number of new rare isotopes have been found amongst the complex elements. In other cases some atomic species reported previously have not been detected, such as the three isotopes of lead, 205, 209, and 210.

Since his values are regarded by the Committee on Atoms of the International Union as superseding the older ones, it is satisfactory to note that these new ratios lead to atomic weights differing in most cases but slightly from the international figures: osmium was a striking exception and its atomic weight has been corrected.

Nier¹¹ also reports that he has found the isotopic constitution of common lead to vary appreciably in twelve samples of known origin and of different geological age. In most of these the computed atomic weight agrees satisfactorily with the chemical value previously determined from the same sample, but it is evident that lead of constant isotopic composition is not invariably found even in the oldest formations, and that its atomic weight may vary within small limits. Nier attributes the variation to contamination with radiogenic leads present in igneous rocks.

Many other measurements of isotopic abundance ratios have been made recently, notably for Pd, Pt, Ir, Rh, and Co, by M. B.

⁵ See J. Mattauch, *Physikal. Z.*, 1937, **38**, 951; *Z. anorg. Chem.*, 1938, **236**, 209.

⁶ *Rev. Mod. Physics*, 1937, **9**, (3).

⁷ *Ibid.*, 1936, **50**, 1041; see also *Ann. Reports*, 1937, **34**, 8.

⁸ *Physical Rev.*, 1937, **52**, 133.

⁹ *Ibid.*, 1938, **53**, 282.

¹⁰ *Ibid.*, 1938, **54**, 275.

¹¹ *J. Amer. Chem. Soc.*, 1938, **60**, 1571.

Sampson and W. Bleakney,¹² for the rare earth group by A. J. Dempster,¹³ for Li, K, and Rb by A. K. Brewer,¹⁴ for Pb¹⁶ and Nd¹⁷ by J. Mattauch and V. Hauk. A useful summary of work up to the end of 1937 is given by Otto Hahn.¹⁸

In view of this rapid progress, it would be premature to attempt to correlate in detail the physical and chemical data, but the significance of the former in relation to the chemical atomic weights is evident.

It is well to bear in mind that isotopic weights deduced from mass spectra may, as Aston¹⁹ has emphasised, be affected by cumulative errors especially when they are based on a long chain of relationships. The same applies even more to the calculation from energy relations. There is, however, a high probability that a final result has been reached when the chemical and physical values agree closely.

The cases of cadmium²¹ and tellurium,²⁰ for which, on account of errors in the mass spectrum, the chemical values have been found to be nearer the truth, have been mentioned in earlier reports. Another instance is neodymium,²² for which the mass spectrum value, Nd = 143.5, is less than the chemical value, Nd = 144.27, founded on the work of G. P. Baxter and H. C. Chapin²³ in 1911 by nearly 0.8 unit. A careful revision by O. Hönigschmid and F. Wittner,²⁴ who compared anhydrous neodymium chloride with silver by the standard procedure, has been published recently and gave Nd = 144.273. The discovery of two new isotopes by A. J. Dempster,²⁵ viz., ¹⁴⁸Nd and ¹⁵⁰Nd, does not explain the discrepancy, for they are only present in small amounts. J. Mattauch and V. Hauk²⁶ have now revised the isotopic constitution of this element, using a more developed technique, and their measurements give Nd = 144.29 ± 0.03 and thus bring the two values into satisfactory agreement. Among the rare earths, holmium²² still presents an outstanding discrepancy; lesser differences are shown by samarium, thulium, and terbium. Chemical revision of gadolinium²⁷ and erbium²⁸ has brought about a close agreement. The new work of

¹² *Physical Rev.*, 1936, **50**, 732.

¹⁸ *Ibid.*, 1938, **53**, 727.

¹⁴ *Ibid.*, 1936, **49**, 867.

¹⁵ *Ibid.*, 1937, **52**, 885.

¹⁶ *Naturwiss.*, 1937, **25**, 763.

¹⁷ *Ibid.*, p. 780.

¹⁸ *Ber.*, 1938, **71**, 1.

¹⁹ *Nature*, 1935, **135**, 541.

²⁰ *Ann. Reports*, 1934, **31**, 95.

²¹ *Ibid.*, 1936, **33**, 142.

²² *Ibid.*, 1934, **31**, 370, 94; *Proc. Roy. Soc.*, 1934, **A**, **146**, 46.

²³ *J. Amer. Chem. Soc.*, 1911, **33**, 1.

²⁵ *Physical Rev.*, 1937, **51**, 289.

²⁴ *Z. anorg. Chem.*, 1938, **235**, 220.

²⁶ *Naturwiss.*, 1937, **25**, 780.

²⁷ *Ann. Reports*, 1936, **33**, 135; C. R. Naeser and B. S. Hopkins, *J. Amer. Chem. Soc.*, 1935, **57**, 2183.

²⁸ O. Hönigschmid and F. Wittner, *Z. anorg. Chem.*, 1937, **232**, 113.

G. P. Baxter and F. D. Tuemmler²⁹ and of W. Kapfenberger³⁰ on the analysis of europous chloride does not show as close a concordance as is to be expected, though it is clear that the true value for europium lies below 152, the present international figure.

An example of finer differences is that of carbon. The international value for this element was in 1936 changed from 12.00 to 12.01 on the evidence of gas-density measurements which indicated a value greater than 12.00. Mass-spectrograph data from reliable and independent sources, although confirming 12.01, do not give values agreeing to the third place of decimals. Aston's³¹ latest value for ^{12}C on the ^{16}O scale is 12.00355, a result from a number of very carefully checked doublet measurements. E. B. Jordan and K. T. Bainbridge,³² however, find $^{12}\text{C} = 12.00398$, a difference approaching 1 part in 20,000. The latter value is supported by evidence from nuclear-energy changes.^{6, 33} From the viewpoint of the chemist this difference is, however, small. A larger uncertainty lies in the abundance ratio $^{12}\text{C} : ^{13}\text{C}$ of the two isotopes. Aston's value for this is $140 \pm 14 : 1$, found some years ago. More recent measurements give lower values. Thus A. R. Brosi and W. D. Harkins,³⁴ from measurement of the relative intensities of the band heads in the Swan spectrum, find $92.2 \pm 3.7/1$. F. A. Jenkins and L. S. Ornstein³⁵ by a similar method found $106 \pm 11/1$, whilst A. L. Vaughan, J. H. Williams and J. T. Tate³⁶ with the mass spectrograph obtained $91.6 \pm 2.2/1$. Aston's figure, however, is still the international value. The chemical atomic weight calculated from Aston's data, the factor 1.000275³⁷ being used to convert to the chemical scale, is $\text{C} = 12.0074$, whilst a $^{12}\text{C}/^{13}\text{C}$ ratio of 92 combined with the figure of Bainbridge and Jordan gives $\text{C} = 12.0115$. The limiting-pressure method used with the density microbalance gives for the gases oxygen, carbon monoxide and dioxide, and ethylene³⁶ values in substantial agreement with the latter figure, *i.e.*, $\text{C} = 12.010$. E. Moles,³⁸ however, using the standard method of limiting densities but with an improved technique, finds for a comparison of the same gases with oxygen $\text{C} = 12.0070$.

The completion of two important investigations on the chemical

²⁹ *J. Amer. Chem. Soc.*, 1938, **60**, 602. ³⁰ *Z. anorg. Chem.*, 1938, **236**, 273.

³¹ *Proc. Roy. Soc.*, 1937, *A*, **163**, 403. ³² *Physical Rev.*, 1937, **51**, 384.

³³ M. S. Livingston and H. A. Bethe, *Rev. Mod. Physics*, 1937, **9**, 246; see also J. Mattauch and R. Herzog, *Naturwiss.*, 1937, **25**, 147.

³⁴ *Physical Rev.*, 1937, **52**, 472.

³⁵ *Proc. K. Akad. Wetensch. Amsterdam*, 1932, **35**, 1212.

³⁶ *Ann. Reports*, 1936, **33**, 144.

³⁷ W. R. Smythe, *Physical Rev.*, 1934, **45**, 299.

³⁸ *Bull. Soc. chim. Belg.*, 1938, **47**, 427.

side has recently supplied strong evidence in favour of the higher figure. G. P. Baxter and A. H. Hale,³⁹ by the combustion in oxygen over a platinum catalyst of carefully purified specimens of chrysene, $C_{18}H_{12}$, triphenylbenzene, $C_{24}H_{18}$, and anthracene, $C_{14}H_{10}$, have obtained a series of 27 values for carbon ranging from 12.0080 to 12.0118. Quantities of hydrocarbons of 3—6 g. were used in each experiment. The final value with all corrections made is $C = 12.0102$ ($H = 1.0081$). In this work carbon is compared directly with oxygen. A. F. Scott and F. H. Hurley, jun.,⁴⁰ have determined the ratio of benzoyl chloride to silver. The benzoyl chloride, prepared from highly purified benzoic acid from thiophene-free toluene, and phosphorus trichloride, was fractionally distilled in a vacuum in an all-glass apparatus. The silver equivalent of the various final fractions was determined by the standard opalescence method. The mean is computed from eight closely concordant values, the extremes being 12.0099 and 12.0106. The final mean with $H = 1.0081$ is $C = 12.0100$. The evidence from all these sources makes the higher value more probable, and the international committee in their Eighth Report assign to carbon the value 12.010. A. F. Scott and F. H. Hurley, jun.,⁴¹ have also pointed out that the new value for carbon leads to a slightly lower value for sodium in the ratios $Na_2CO_3/2Ag$, $Na_2CO_3/2AgBr$, and Na_2CO_3/I_2O_5 , the mean giving $Na = 22.993$ in agreement with the value $Na = 22.994$ found by C. R. Johnson,⁴² and lower than the accepted value by 0.004 unit.

The atomic weight of phosphorus, to which attention was directed in the Annual Report for 1934, has quite recently been redetermined by the analysis of phosphorus oxychloride by O. Hönigschmid and W. Menn.⁴³ The preparation of this substance in a high state of purity was accomplished by first subjecting the commercial product to fractional distillation to remove the greater part of the trichloride, followed by treatment of the product with phosphoric anhydride to eliminate any pentahalide, and subsequent fractional recrystallisation. The material so obtained was distilled in a vacuum through a fractionating column in a sealed glass apparatus a number of times, until the fractions gave closely concordant results on analysis. The sealed bulbs containing the final oxychloride were, after weighing, broken below the surface of aqueous ammonia in a stoppered flask, the glass fragments collected on a fritted filter, weighed, and the chlorine content of the solution determined by standard methods. The results give values for the atomic weight

³⁹ *J. Amer. Chem. Soc.*, 1937, **59**, 506.

⁴⁰ *Ibid.*, p. 1905.

⁴¹ *Ibid.*, p. 2078.

⁴² *Ann. Reports*, 1935, **32**, 95.

⁴³ *Z. anorg. Chem.*, 1937, **235**, 129.

from the two ratios $\text{POCl}_3 : 3\text{Ag} : 3\text{AgCl}$ varying from 30.986 to 30.975, with a final mean of $P = 30.978$ when $\text{Cl} = 35.475$ and $\text{Ag} = 107.880$. The current value $P = 31.02$ is based on the analysis of the trichloride and tribromide carried out 25 years ago by Baxter and his collaborators.⁴⁴ Since this element is single and no rare isotopes have been reported, and moreover, its packing fraction is accurately known, any uncertainty has been removed by the close agreement of the chemical with the physical figure $P = 30.975$, calculated from Aston's recent value with the factor 1.000275. This again accords very closely with $P = 30.977$ found from the limiting density of phosphine in 1930 by M. Ritchie⁴⁵ as a result of very careful measurements.

The claim of A. K. Brewer to have proved that plants assimilate selectively the ^{41}K isotope was noted in 1936.⁴⁶ He⁴⁷ now finds that the potassium from some animal tissues shows a similar displacement of the $^{39}\text{K}/^{41}\text{K}$ ratio. These observations so far are without independent confirmation. That the rare ^{40}K isotope is responsible for the radioactivity of this element has been proved by W. R. Smythe and A. Hemmendinger⁴⁸ and confirmed by others.⁴⁹

It seems likely that ^{40}K disintegrates by a dual change to ^{40}Ca and ^{40}Ar , and that the bulk of the argon in the atmosphere has been formed in this way.^{49, 50} An interesting account of all this work is given by Brewer.⁴⁷

Equally interesting is recent work on the other naturally radioactive alkali metal rubidium, the β -radiation from which has been shown to be due to the less abundant of its two isotopes,^{51 viz.}, ^{87}Rb . The ratio $^{85}\text{Rb}/^{87}\text{Rb}$ has been determined by A. K. Brewer⁵² in minerals from various localities and he found no appreciable variation. His value 2.61 is rather lower than A. O. Nier's 2.68, and he calculates the atomic weight to be $\text{Rb} = 85.456$. The international value is $\text{Rb} = 85.48$, based on the ratios $\text{RbCl} : \text{Ag}$ and $\text{RbBr} : \text{Ag}$ determined by standard methods in 1936 by E. H. Archibald and J. G. Hooley.⁵³ ^{87}Rb disintegrates to ^{87}Sr , and O. Hahn, F. Strassmann, and E. Walling,⁵⁴ from 1 kg. of a Canadian

⁴⁴ G. P. Baxter, C. J. Moore, and A. C. Boylston, *Z. anorg. Chem.*, 1912, **74**, 365; G. P. Baxter and C. J. Moore, *ibid.*, 1913, **80**, 185.

⁴⁵ *Proc. Roy. Soc.*, 1930, *A*, **128**, 551.

⁴⁶ *Ann. Reports*, 1936, **33**, 140.

⁴⁷ *Ind. Eng. Chem.*, 1938, **30**, 893.

⁴⁸ *Physical Rev.*, 1937, **51**, 178.

⁴⁹ C. F. Weizsäcker, *Physikal. Z.*, 1937, **38**, 623; A. Bramley and A. K. Brewer, *Physical Rev.*, 1938, **53**, 502.

⁵⁰ A. Bramley, *Science*, 1937, **86**, 424.

⁵¹ J. Mattauch, *Physikal. Z.*, 1937, **38**, 958; W. R. Smythe and A. Hemmendinger, *Physical Rev.*, 1937, **51**, 1052; W. Walcher, *Physikal. Z.*, 1937, **38**, 961.

⁵² *J. Amer. Chem. Soc.*, 1938, **60**, 691.

⁵³ *Ibid.*, 1936, **58**, 70, 618.

⁵⁴ *Naturwiss.*, 1937, **25**, 189.

lithium mica containing rubidium, have isolated 250 mg. of strontium carbonate, which J. Mattauch ⁵⁵ proved by examination with the mass spectrograph to consist almost entirely of ⁸⁷Sr. The principal constituents of strontium are the three isotopes 86, 87, and 88 in the approximate proportions of 10, 7, and 83%. The isotopic weight of ⁸⁷Sr on the chemical scale is 86.90. The atomic weight of the element is 87.63. The separation of larger amounts of the practically pure isotope will enable the isotopic weight to be determined by chemical analysis. It is evident that strontium extracted from minerals containing rubidium will have an atomic weight below the normal value.

The difference in the atomic weights of oxygen from water and from air, first reported by M. Dole and confirmed by N. Morita and T. Titani,⁵⁶ has again been confirmed. E. R. Smith and H. Matheson ⁵⁷ find that water containing oxygen from air is 8.6 parts per million heavier than that containing oxygen derived from water. T. O. Jones and N. F. Hall,⁵⁸ from an exchange reaction on platinum above 1800°, find 7 p.p.m. Dole found a difference of 6 and Morita and Titani 7 p.p.m.

Further data have appeared on the deuterium content of normal water. J. L. Gabbard and M. Dole ⁵⁹ find H/D = 6900/1 in Lake Michigan water, N. Morita and T. Titani,⁶⁰ in tap water from Osaka and from Cambridge, U.S.A., 6200/1, and L. Tronstad and J. Brun,⁶¹ in water from Rjukan, 5960/1. The mean value approximates to 6000/1, rather greater than earlier estimates but not sufficient to affect the fourth decimal place in calculating the atomic weight of chemical hydrogen from mass-spectrum analysis.

The relative abundance of the oxygen isotopes ¹⁶O and ¹⁸O is now considered to be expressed more exactly by the value 530 ± 10 found by W. R. Smythe ⁶² than by the older value of R. Mecke and W. H. J. Childs, viz., 630 ± 60 .⁶³ The factor for correction to the chemical scale hence becomes 1.000275.

In the last two years a number of papers have been published by E. Moles and his pupils ^{38, 64} on normal and limiting densities of gases and the atomic weights derived from them. Moles has

⁵⁵ *Naturwiss.*, 1937, **25**, 170, 189.

⁵⁶ See *Ann. Reports*, 1936, **33**, 141.

⁵⁷ *J. Res. Nat. Bur. Stand.*, 1936, **17**, 625.

⁵⁸ *J. Amer. Chem. Soc.*, 1937, **59**, 259.

⁵⁹ *Ibid.*, p. 181.

⁶⁰ *Bull. Chem. Soc. Japan*, 1938, **13**, 419.

⁶¹ *Trans. Faraday Soc.*, 1938, **34**, 766.

⁶² *Physical Rev.*, 1934, **45**, 299.

⁶³ *Z. Physik*, 1931, **68**, 362.

⁶⁴ E. Moles and T. Toral, *Monatsh.*, 1936, **69**, 342; E. Moles and J. Sancho, *Anal. Fis. Quím.*, 1934, **32**, 931; 1936, **34**, 865; E. Moles, *J. Chim. physique*, 1937, **34**, 49; *Compt. rend.*, 1937, **205**, 1391; E. Moles and C. Roquero, *Anal. Fis. Quím.*, 1937, **35**, 263; E. Moles and A. Escribano, *Compt. rend.*, 1938, **207**, 66; E. Moles and T. Salazar, *Anal. Fis. Quím.*, 1934, **32**, 954.

greatly improved the technique of the standard methods, and takes elaborate precautions to avoid small errors. For instance, rubber connexions carrying mercury are dispensed with. The mercury in the manometer and the gas-leading tubes is kept at a constant temperature either by water circulating from a thermostat or by immersion in ice. Mercury never comes in contact with tap grease. No gas other than pure dry air ever enters the lower manometer chamber, and the gas pressure in the density bulbs or volumeter is equalised through a gauge filled with Apiezon oil. The employment of fritted-glass filters prevents any oil or mercury fog from entering the density bulbs. Adsorption is measured for each gas on glass of the same composition as the density bulbs, and a correction appropriate to the filling pressure is applied. Moles claims to reach an accuracy of about 1 part in 10^5 in his density values. This is borne out by his work on oxygen.

Since 1933 he has published with his co-workers five papers on the density of this standard gas and made 99 determinations of the normal litre weight. The results, which agree to a very close approximation, give as a mean the value 1.42894 ± 0.00001 at 0° , sea level, lat. 45° ($g = 980.616$).

In these investigations there is always the possibility that the limiting density values are affected by errors due to the form taken by the pv - p graph in extrapolating to zero pressure. There is no uncertainty about the permanent gases, the pv - p values of which are linear to a high degree, but with gases such as ammonia, sulphur dioxide, and carbon dioxide, which are easily liquefied, strictly linear relationship cannot be assumed without strong evidence.

A critical discussion ⁶⁵ of this and of other sources of error, and also of modern work on the physicochemical determination of the molecular and atomic weights of gases, has just been published by the Institut International de Cooperation Intellectuelle as the result of a meeting of a number of workers in this field.

From general theoretical considerations, it would appear that the pv - p isothermals for liquefiable gases are slightly curved, the slope of the graph becoming smaller towards lower pressures. This curvature is small even with a gas like carbon dioxide, but W. H. Keesom ⁶⁶ contends that it must be allowed for when results of the highest accuracy are required, and that the second term in equations of the type $pv = A + Bp + Cp^2$, etc., which represents the behaviour of gases at high pressures, is of significance from 1 atmosphere downwards.

⁶⁵ "Les Determinations physico-chimiques des Poids Moleculaires et Atomiques des Gaz," Paris, 1938.

⁶⁶ *Ibid.*, pp. 105—109 and 165.

Direct experimental results in the neighbourhood of 1 atmosphere, such as those of W. Cawood and H. S. Patterson,⁶⁷ appear to give a linear pv - p relationship. It is doubtful, however, whether any data are yet available of sufficient accuracy to detect a slight curvature with certainty. W. H. Keesom points out that Moles' results for carbon dioxide, ammonia, and silane, when extrapolated on a pv - p basis, although apparently linear, can be represented equally well by an equation of the second degree. Moles,⁶⁸ however, finds that the *densities* per unit pressure of all the liquefiable gases examined, *i.e.*, carbon dioxide, ethylene, silicon tetrafluoride, and ammonia, are a linear function of p to a high order of accuracy over the pressure range from 1 to 1/4 atmosphere.

The extrapolation of the "litre weights" determined at pressures from 1 to 1/4 atmosphere and reduced afterwards to unit pressure, *i.e.*, 1 atmosphere, as a linear function of p is not equivalent to a linear extrapolation of pv . The first assumes W/pv and the second pv/W to be linear, where W is the weight of the gas in litres filling the density bulb at 0°. They cannot both be linear. Actually, the differences between the two methods of extrapolation are small, and again it may be doubted whether the accuracy of the experimental data is sufficient to decide between them. D. Berthelot's original assumption was that, for the permanent gases at least, pv - p was strictly linear. Nobody would wish to dispute this now, but further experimental work of a high order of precision on the compressibilities of the liquefiable gases is clearly desirable. The method of "limiting pressures"⁶⁹ would appear in this connexion to be superior to that of "limiting densities" since it allows gases to be compared at lower pressures and so avoids so long an extrapolation. In comparison with the older methods it has the sole disadvantage that the microbalance requires a careful surface compensation to eliminate the effect of adsorption on account of the greater ratio of surface to volume in small bulbs. On the other hand, adsorption on vitreous silica is less than on glass.

In the publication cited⁶⁵ new results for silane and hydrogen sulphide are reported by R. Whytlaw-Gray and W. Cawood and by Cawood; using the silica microbalance, they give $\text{Si} = 28.112$ and $\text{S} = 32.065$.

E. Moles also reports fresh results with ammonia,⁷⁰ silicon tetrafluoride,⁷¹ sulphur dioxide,⁷² and hydrogen sulphide. From

⁶⁷ *J.*, 1933, 619.

⁶⁸ *Op. cit.*, pp. 185—192.

⁶⁹ W. Cawood and H. S. Patterson, *Phil. Trans.*, 1936, **A**, 236, 77.

⁷⁰ E. Moles and J. Sandro, *Anal. Fis. Quim.*, 1936, **34**, 865.

⁷¹ E. Moles and T. Toral, *Z. anorg. Chem.*, 1938, **236**, 225.

⁷² E. Moles, T. Toral, and A. Escribano, *Compt. rend.*, 1938, **206**, 1726.

the limiting densities, he finds $S = 32.062$ (SO_2), $S = 32.065$ (H_2S), $N = 14.008$, and $F = 18.995$. A. O. Nier from his abundance ratios finds $S = 32.064$.

In calculating the value for fluorine from silicon fluoride, Moles takes $\text{Si} = 28.104$, a value distinctly greater than the international value $\text{Si} = 28.06$, but which is supported by the work of P. F. Weatherill and P. S. Brundage⁷³ and also by that of O. Hönigschmid and M. Steinheil.⁷⁴ The mass-spectrum value is $\text{Si} = 28.12$, calculated from Aston's latest values for ^{28}Si and ^{29}Si , for ^{30}Si the value from energy changes and for the abundance ratios the figures given in the third report of the Committee on Atoms of the International Union.⁷⁵ If reliance can be placed on the accuracy of the abundance ratios the current value for the atomic weight of silicon would appear to be too low.

In addition to the investigations mentioned, new chemical work on the atomic weights of the following elements has also been published during the period under review : arsenic,⁷⁶ aluminium,⁷⁷ radiogenic leads,⁷⁸ lead,⁷⁹ lutecium,⁸⁰ and ruthenium.⁸¹

R. W.-G.

3. THE SEPARATION OF ISOTOPES.

Since F. W. Aston's announcement in 1913 that a partial separation of the isotopes of neon had been effected, many attempts to separate the isotopes of the stable elements have been made. The work done in this field up to 1933 has been reviewed by Aston,¹ and his survey of the separations actually achieved to that date " shows that from the practical point of view they are, with two exceptions very small. In cases where the method can deal with fair quantities of the substance, the order of the separation is small, while in the case of complete separation the quantities produced are insignificant." The two exceptions referred to by Aston are the separation of the neon isotopes by continuous diffusion and of the hydrogen isotopes by electrolysis. The progress made in separating hydrogen and deuterium has been described in recent Annual Reports² and

⁷³ *J. Amer. Chem. Soc.*, 1932, **54**, 3932.

⁷⁴ *Z. anorg. Chem.*, 1924, **141**, 101.

⁷⁵ *J.*, 1938, 1110.

⁷⁶ J. H. Křepelka and M. Kočnar, *Coll. Czech. Chem. Comm.*, 1936, **8**, 485.

⁷⁷ J. I. Hoffmann and G. E. F. Lundell, *J. Res. Nat. Bur. Stand.*, 1937, **8**, 1.

⁷⁸ G. P. Baxter, J. H. Faull, jun., and F. D. Tuemmler, *J. Amer. Chem. Soc.*, 1937, **59**, 702; G. P. Baxter and W. M. Kelley, *ibid.*, 1938, **60**, 62.

⁷⁹ J. P. Marble, *ibid.*, 1937, **59**, 653.

⁸⁰ O. Hönigschmid, *Naturwiss.*, 1937, **25**, 748.

⁸¹ K. Gleu and K. Rehm, *Z. anorg. Chem.*, 1938, **235**, 352.

¹ "Mass Spectra and Isotopes," 1933, pp. 219—233.

² *Ann. Reports*, 1935, **32**, 41; 1937, **34**, 32.

will not come within the scope of the present article. The successful separation of the hydrogen isotopes by means of electrolysis and diffusion undoubtedly stimulated the efforts to increase the separation of the isotopes of other elements, and considerable progress in this direction has been made since the publication of Aston's survey. The ultimate goal of complete separation, however, has been achieved with only a very limited number of elements. An excellent summary of the results obtained up to 1936 has been published by G. Champetier.³

Although the methods leading to the partial or complete separation of isotopes are of interest in themselves, there are many important applications of the results of such separations in chemistry, physics, and biology. In the first place one may quote Aston's remark⁴ that "in physics all constants involving, *e.g.*, the density of mercury or the atomic weight of silver may have to be redefined, while in chemistry reconstruction may be necessary for that part of the science the numerical foundations of which have hitherto rested securely upon the constancy of atomic weights." According to H. C. Urey and L. J. Greiff,⁵ owing to the possibility of isotopic separation occurring in chemical reactions, there is a "limit to the precision with which atomic weights may be determined and this limit has already been reached for several of the lighter elements." There are, moreover, many problems in the fields of nuclear transformations, radioactivity, and spectroscopy which can be completely or partly solved by using separated isotopes. The use of fractionated isotopes as indicators in the study of chemical exchange reactions and biological processes is becoming of increasing importance, and in this type of work even partly separated isotopes will in many cases provide a useful tool. It should be borne in mind that what is meant by an appreciable separation "depends upon the uses for which the isotopic mixtures are being prepared. If the principal purpose is to study the properties of pure isotopic compounds a nearly complete separation is desired. On the other hand, if they are to be used as tracers or for studying many exchange reaction problems, the extent of the separation is determined by the dilution factor in the experiments and the sensitiveness of the method of analysis."⁶ Another factor of practical importance is the length of time required to effect a separation of amounts of material which are sufficient for the special application.

In the literature dealing with the separation of isotopes, the

³ *Bull. Soc. chim.*, 1936, **3**, 1701; cf. also *Ann. Reports*, 1937, **34**, 43; 1935, **32**, 51.

⁴ *Op. cit.*, p. 219.

⁵ *J. Amer. Chem. Soc.*, 1935, **57**, 321.

⁶ H. C. Urey, J. R. Huffman, H. G. Thode and M. Fox, *J. Chem. Physics*, 1937, **5**, 857.

extent of separation of a mixture of two isotopic elements or compounds is commonly expressed quantitatively by means of a separation or fractionation factor. If, for example, n_1 and n_2 are the numbers of light and heavy atoms in a mixture before, and N_1 and N_2 the corresponding numbers after, a single separation process, then, if $N_1/N_2 > n_1/n_2$, the separation factor for the light isotope is defined as $q = (N_1/N_2)/(n_1/n_2)$. This simple-process separation factor must be distinguished from the total or over-all enrichment factor, A , which expresses the results of a number of successive separation stages. In general, if there are x single stages, $A = q^x$.

It will be convenient to deal in turn with the more important separation methods and to describe briefly the results achieved in each case, with special reference to the period since 1933.

(1) *Separation by Means of Mass-ray Analysis.*—It was realised quite early that one of the most promising methods for the complete separation of isotopes would consist in the adaptation of the mass spectrograph itself for this purpose. In the ordinary forms of this instrument separation of the atoms according to their masses does occur, but the amounts which are separated even in a few hours are very small since the positive-ion beams are of the order of 10^{-8} amp. or less. Attention has been directed, therefore, to increasing the ion beam capacity. The earlier attempts of M. Morand ⁷ to separate the isotopes of lithium and of K. P. Jakowlew ⁸ to separate those of neon by mass-spectrograph methods did not give any significant separation.

The first successful results by this method were obtained in 1934 by M. L. Oliphant, E. S. Shire, and B. M. Crowther ⁹ in the Cavendish laboratory, and by W. R. Smythe, L. H. Rumbaugh, and S. S. West ¹⁰ in California. The Cambridge workers described two mass spectrographs using the combined action of crossed electrostatic and magnetic fields, by means of which the isotopes ^6Li and ^7Li were separated in quantities of about 10^{-8} g. The lithium ions were obtained from a platinum filament coated with a mixture of $3\text{Li}_2\text{CO}_3, \text{Al}_2\text{O}_3, 3\text{SiO}_2$ and activated by preliminary heat treatment. An ion current of several hundred micro-amps. could be taken from such a source for several hours. In one form of the apparatus the beam of lithium ions was passed through a magnetic field of 4000 gauss and an electric field, which was so adjusted as to allow the ions of one isotope to follow a straight path through the narrow channel formed by the edges of the electrically charged plates,

⁷ *Compt. rend.*, 1926, **182**, 460; *Ann. Physique*, 1927, **7**, 164.

⁸ *Z. Physik*, 1930, **64**, 378.

⁹ *Proc. Roy. Soc.*, 1934, **146**, 922.

¹⁰ *Physical Rev.*, 1934, **45**, 724.

while the ions of the other isotope were deflected and prevented from passing out of the end of the channel. The isotopes were collected one at a time on small metal plates carried on a glass tube filled with liquid nitrogen. After collection, the isotopes were fixed by admitting a puff of hydrogen chloride into the apparatus to form lithium chloride. The completeness of the separation effected was confirmed by bombardment experiments with protons and deuterons, the range and nature of the resulting particles being characteristic of the particular isotope.

In the high-intensity mass spectrometer devised by the American workers, positive ions from an extended source of comparatively large area were focused electrostatically to form a nearly plane beam, which was then passed through a magnetic field whose boundaries were so shaped that all particles of a certain mass were focused on a slit beyond the field. The highest convenient ion current obtainable was 0.1 milliamp., which deposited 1 mg. of ^{39}K in 7 hours. Practically complete separation from ^{41}K was obtained. In similar experiments with lithium ions, several samples of ^6Li and ^7Li of about 1 $\mu\text{g.}$ were collected. Quantities of 18 $\mu\text{g.}$ of ^6Li and 200 $\mu\text{g.}$ of ^7Li were also prepared by L. H. Rumbaugh and L. R. Hafstad¹¹ for disintegration experiments.

An interesting application of the use of pure isotopes separated by means of a high-intensity mass spectrometer is furnished by the work of W. R. Smythe and A. Hemmendinger,¹² who were able to obtain quantities of the order of several mg. of the three isotopes of potassium having mass numbers 39, 40, and 41. Activity measurements with these samples showed that only ^{40}K is radioactive. The same workers¹³ further improved the resolving power of their instrument and separated the isotopes of rubidium. Measurements of the radioactivity of samples collected at masses 84, 86, 87, 88, and 90 proved that only ^{87}Rb is active. W. Walcher¹⁴ has also described a mass spectrograph of high intensity by means of which samples of 90 $\mu\text{g.}$ of ^{85}Rb and of 30 $\mu\text{g.}$ of ^{87}Rb were collected in about 15 hours. In this case the purity of the products was shown by investigation of the hyperfine structure of the RbI resonance line at 7800 \AA .

An improved but still comparatively simple mass spectrograph, similar to those described by M. L. Oliphant and his co-workers, has been used recently by E. L. Yates¹⁵ for the separation of 30 $\mu\text{g.}$ of ^7Li and of 2 $\mu\text{g.}$ each of ^{10}B and ^{11}B , as well as for the preparation

¹¹ *Physical Rev.*, 1936, **50**, 681.

¹² *Ibid.*, 1937, **51**, 178.

¹³ *Ibid.*, p. 1052.

¹⁴ *Physikal. Z.*, 1937, **38**, 961; *Z. Physik*, 1938, **108**, 376.

¹⁵ *Proc. Roy. Soc.*, 1938, **168**, 148.

of several μg . of ^{12}C free from ^{13}C . The separated isotopes obtained in these experiments were examined in disintegration experiments and found to be very pure.

Summing up the work carried out so far on the separation of isotopes by the use of high-capacity mass spectrographs, it may be said that the method gives separated isotopes of a high degree of purity. Although the yields obtained are small and of no use for chemical experiments, they are sufficiently large to be of value for many physical purposes.

(2) *Separation by Means of Diffusion Methods.*—(a) *Hertz's method.* Since the rate of diffusion of gases through an aperture which is small in comparison with the mean free path of the molecules is inversely proportional to the square root of the mass of the molecules a change in composition must occur when two or more gases which differ in molecular weight are allowed to diffuse through such an aperture. This was the principle first applied by Aston in his early attempts to separate the isotopes of neon of masses 20 and 22. Diffusion was allowed to take place through a porous material such as pipe-clay. The difference in mass of the components of an isotopic mixture is in general small, and only a very slight separation is obtained in a single process. Fractionation methods must therefore be resorted to. The weakness of the earlier diffusion experiments of Aston and of others lay in the use of only one fractionation unit in a single operation. The technique was enormously improved in 1932 by G. Hertz,¹⁶ who introduced the use of porous-walled diffusion units so designed that a number of them could be used in series. Mercury-diffusion pumps were incorporated in the apparatus to circulate the gases through the various units, thus making the whole process continuous and automatic. At one end of the series of pumps the gas becomes enriched with respect to the heavier component; at the other end it is enriched with respect to the lighter constituent. Since the system is a closed one, eventually a state of equilibrium is reached in which the composition of the gas mixture circulating in the various units changes progressively from one unit to the next. As the total separation factor increases exponentially with the number of units, in principle any desired separation can be obtained by using a sufficient number of them.

With his first apparatus consisting of 24 units Hertz was able to obtain, in addition to the results with hydrogen, a considerable separation of the two main isotopes of neon. A later apparatus,¹⁷ using about 50 stages, by means of which pure hydrogen and

¹⁶ *Z. Physik*, 1932, **79**, 108.

¹⁷ H. Harmsen, *ibid.*, 1933, **82**, 589; H. Harmsen, G. Hertz, and W. Schütze, *ibid.*, 1934, **90**, 703.

deuterium were prepared, also gave practically pure ^{22}Ne . D. E. Wooldridge and F. A. Jenkins¹⁸ have described a similar apparatus containing 34 porous-walled units with which they obtained gaseous methane having 16% of $^{13}\text{CH}_4$ instead of the normal 1%. They have also reported the concentration by this method of ^{15}N in nitrogen from the normal 0.6% to 6%.

The difficulty of preventing the accumulation of impurities during operation of the porous-walled units led G. Hertz¹⁹ to modify the technique of the diffusion method. In the more recent forms of apparatus the porous tubes are dispensed with, and use is made of the stream of mercury vapour in the pump as the diffusion medium. The essential principle of the modified Langmuir pump devised by Hertz is that only the centre portion of the stream of mercury vapour is used to pump away the gas, which has to diffuse through the mercury vapour stream in a direction perpendicular to it. The greater the diffusion velocity of the gas, the more it will penetrate into the centre of the mercury vapour stream, which will therefore be enriched with respect to the lighter component of the gas. Apart from this modification in the nature of the diffusion medium, the technique of the newer method is much the same as in the porous-walled type, and a large number of pumps is used in series. The same over-all separation factor is achieved in a shorter time in the newer apparatus. The degree of enrichment will depend, of course, on certain factors, such as the diffusion constant of the gas being used, the streaming velocity of the mercury vapour, and the geometrical dimensions of the pumps.^{20, 21, 22} Under the best operating conditions the Hertz method is able to produce highly concentrated or even completely separated materials, but the yields are only of the order of a few c.c. (at N.T.P.) of enriched gas per 24 hours' operation.

With the newer apparatus, G. Hertz¹⁹ obtained a marked separation of the isotopes ^{20}Ne and ^{22}Ne . Using a similar method, H. Barwich and W. Schütze²³ separated normal argon ($^{40}\text{A} : ^{38}\text{A} : ^{36}\text{A} = 99.64 : 0.06 : 0.30$) into light and heavy fractions, which were found by means of mass-spectrograph analysis to contain 90.89, 0.51, 8.6 and 99.74, 0.046, 0.23%, respectively, of the three isotopes. H. Kopfermann and H. Krüger,²⁴ with the same apparatus, carried out a 300-hour run in which the volume of gas at the

¹⁸ *Physical Rev.*, 1936, **49**, 404, 704; cf. also D. E. Wooldridge and W. R. Smythe, *ibid.*, 1936, **50**, 233.

¹⁹ *Z. Physik*, 1934, **91**, 810.

²⁰ H. Barwich, *ibid.*, 1936, **100**, 166.

²¹ R. Scherr, *J. Chem. Physics*, 1938, **6**, 251.

²² D. MacGillavry, *Rec. Trav. chim.*, 1937, **56**, 330; *Trans. Faraday Soc.*, 1937, **33**, 433.

²³ *Z. Physik*, 1937, **105**, 395.

²⁴ *Ibid.*, 1937, **105**, 389.

"heavy" end was replaced every 6 hours by normal argon. From 1 litre of normal argon (at 700 mm. pressure) they obtained 500 c.c. (at 1 mm. pressure) of a mixture containing ^{36}A and ^{40}A in the ratio 1 : 1. H. Krüger,²⁵ by diffusion of a sample of nitrogen containing about 1.9% of ^{15}N , got a product in which the concentration of the heavy nitrogen was increased to 20%. A battery of 51 Hertz pumps has also been used²⁶ to obtain a partial separation of $^{12}\text{CH}_4$ and $^{13}\text{CH}_4$. A run of 30 hours' pumping yielded 300 c.c. of methane at 1.8 mm. containing about 30% of ^{13}C , as indicated by the intensities of the isotopic Swan bands.

(b) *Gravitational diffusion*. Although the attempts at separating isotopes by centrifuging have been generally abandoned as impracticable, the development of a new air-driven centrifuge has encouraged J. W. Beams and his co-workers²⁷ to re-examine the feasibility of the method. They have announced preliminary attempts to separate the isotopes of chlorine in the form of carbon tetrachloride by a modification of a method first suggested by R. S. Mulliken,²⁸ using a vacuum type tubular centrifuge which separates substances of different molecular weight while in the vapour state. By this means carbon tetrachloride has been separated into light, medium, and heavy fractions, but in the preliminary papers no data are given as to the extent of the separation achieved. The method, however, appears to be a promising one, since the separation is quite fast and comparatively large quantities can be centrifuged.

(c) *Thermal diffusion*. K. Clusius and G. Dickel²⁹ have described partial separations of the isotopes of chlorine in hydrogen chloride and of neon which depend, in part at least, on the application of the principles of thermal diffusion. In their apparatus a vertical hot surface, consisting of an electrically heated wire, is placed opposite a cold surface, and between the two is a gas mixture. As a result of thermal diffusion, the relative concentration of the heavier molecules at the cold surface is greater than at the hot surface. In addition, owing to a thermal syphoning effect, the gas rises at the hot surface, flows over to the cold surface at the top of the column, sinks down the cold surface, and at the foot flows over again to the hot surface. Consequently, two streams of gas are constantly moving past one another which are not in equilibrium with respect

²⁵ *Naturwiss.*, 1938, **26**, 445.

²⁶ P. Capron, J. M. Delfosse, M. de Hemptinne and H. S. Taylor, *J. Chem. Physics*, 1938, **6**, 656.

²⁷ J. W. Beams and F. B. Haynes, *Physical Rev.*, 1936, **50**, 491; J. W. Beams and A. V. Masket, *ibid.*, 1937, **51**, 384; J. W. Beams and L. B. Snoddy, *J. Chem. Physics*, 1937, **5**, 993.

²⁸ *J. Amer. Chem. Soc.*, 1922, **44**, 1033; 1923, **45**, 1592.

²⁹ *Naturwiss.*, 1938, **26**, 546.

to thermal diffusion. The simultaneous working of both processes causes an enrichment of the heavier component at the bottom and of the lighter component at the top of the apparatus. With neon a fraction was obtained from the "heavy" end of the apparatus in which the ratio of $^{22}\text{Ne} : ^{20}\text{Ne}$ had been increased from the normal value of 1 : 9.28 to 1 : 2.20. Normal hydrogen chloride (23% H^{37}Cl , 77% H^{35}Cl) gave a gas consisting of 40% H^{37}Cl and 60% H^{35}Cl at the base of the apparatus

(3) *Separation by Means of Electrochemical Methods.*—The suggestion that isotopes might be separated by electrolysis had been made in 1923 by J. Kendall and E. D. Crittenden.³⁰ Following on the success with hydrogen and deuterium further attempts have been made to separate the isotopes of other elements by the electrolytic method.

The possibility of the electrolytic separation of the oxygen isotopes ^{16}O and ^{18}O (assuming ^{17}O to be negligible in amount) was discussed by E. W. Washburn and H. C. Urey.³¹ In the prolonged electrolysis of ordinary water resulting in an enrichment with respect to D_2O , it is necessary to determine whether all the density increase of the water is due to deuterium or can be ascribed in part to the heavy oxygen isotope. The early experiments in this direction led to rather conflicting results.³² It was shown, however, by P. W. Selwood, H. S. Taylor, J. A. Hipple, and W. Bleakney³³ that the failure of some of the earlier workers to obtain heavy oxygen enrichment in the water resulting from a number of electrolysis stages was due to equilibration of the oxygen isotope ratio in the water to, or nearly to, that of the carbon dioxide used to neutralise the concentrated alkali solutions before distillation. Experiments in which neutralisation was accomplished by means of ammonium chloride or hydrogen chloride showed that when 117 litres of 0.5N-sodium hydroxide were electrolysed with nickel anodes down to 1 c.c., there was a steady but slow increase in concentration of ^{18}O (determined by the mass spectrograph) from 0.202% to 0.222%, i.e., an increase of only 10% corresponding to a separation factor of 1.01. H. L. Johnston³⁴ carried out a fractional electrolysis of potassium hydroxide solution, using iron electrodes which were known to give a large separation of the isotopes of hydrogen. The light water from each stage was obtained by recombining the hydrogen and oxygen from the first 25% of the electrolysis. Since three stages of electrolysis were known to reduce the deuterium content

³⁰ *Proc. Nat. Acad. Sci.*, 1923, **9**, 75.

³¹ *Ibid.*, 1932, **18**, 496.

³² Cf. refs. (33) and (36).

³³ *J. Amer. Chem. Soc.*, 1935, **57**, 642; *Physical Rev.*, 1935, **47**, 800.

³⁴ *J. Amer. Chem. Soc.*, 1935, **57**, 484.

of the recovered gases to a negligible amount, density changes in later stages must result from the electrolytic separation of the oxygen isotopes only. In fact, during the first three or four electrolyses the density of the light water decreased comparatively rapidly, after which there was a slower steady decrease with increasing number of electrolyses. From these experiments the separation factor of ^{18}O from ^{16}O was found to be 1.008. W. H. Hall and H. L. Johnston³⁵ also determined the amount of heavy oxygen in the electrolyte from commercial cells which had been in continuous operation for over seven years. The excess density due to ^{18}O gave a separation factor of 1.008. A somewhat greater value for this separation factor has been obtained by L. Tronstad and J. Brun,³⁶ viz., 1.034, and other values have also been recorded. Undoubtedly, the value of the separation factor will depend on the conditions of electrolysis. It is clear, however, that the electrolytic method is not very practicable for the preparation of water containing heavy oxygen in high concentration. It has been estimated³⁴ that "reduction of the entire ocean by electrolysis to a residual cubic mm. would less than double the concentration of the heavy isotopes of oxygen," unless, of course, electrode materials or other conditions of electrolysis were found which gave a more efficient separation.

The electrolytic method of separating isotopes has been more successful in the case of the element lithium, although in some of the earlier attempts no significant separation was obtained.^{37, 38, 39} Recently, however, T. I. Taylor and H. C. Urey⁴⁰ and L. Holleck⁴¹ have shown that ^6Li is deposited preferentially with respect to ^7Li at a mercury cathode, and have effected a partial but appreciable separation of these two isotopes. Taylor and Urey electrolysed 800 c.c. of a 10% solution of lithium hydroxide in a cell containing a nickel anode above a rapidly stirred mercury cathode, till only about 1 g. of the hydroxide was left in the cell. Mercury was allowed to flow continuously through the cell to remove the lithium amalgam as it was produced. Twenty such runs were carried out, and the residual solutions were united, concentrated, and electrolysed further. The ratio of the initial to the final residual lithium was about 600:1. Mass-spectrograph analysis showed that the

³⁵ *J. Amer. Chem. Soc.*, 1935, **57**, 1515.

³⁶ *Trans. Faraday Soc.*, 1938, **34**, 766; cf. also N. Morita, *J. Chem. Soc. Japan*, 1936, **57**, 176.

³⁷ J. Kendall, *Proc. Roy. Soc. Edinburgh*, 1937, **57**, 182.

³⁸ A. Eucken and K. Bratzler, *Z. physikal. Chem.*, 1935, **A**, **174**, 269.

³⁹ G. Champetier and P. Regnaut, *Bull. Soc. chim.*, 1937, **4**, 592.

⁴⁰ *J. Chem. Physics*, 1937, **5**, 597.

⁴¹ *Z. Elektrochem.*, 1938, **44**, 111.

ratio ${}^7\text{Li} : {}^6\text{Li}$, which was 12.5 : 1 in the hydroxide used, had been increased in the final residue to 14.2 : 1, corresponding to a simple-process separation factor of 1.020. Later experiments⁴² with lithium chloride gave a fractionation factor of 1.039. Holleck also electrolysed a solution of the chloride fractionally at a mercury cathode from which the deposited lithium was continuously removed. He concentrated 9000 g. of lithium chloride in three stages down to a final deposited fraction of 5.6 g., in which the lithium was found to have an atomic weight of 6.894 compared with a value of 6.941 in the original material. These figures correspond to an enrichment of ${}^6\text{Li}$ by 71% of the concentration originally present.

G. N. Lewis and R. T. Macdonald⁴³ have obtained a marked separation of the isotopes of lithium by a method which, though not a direct electrolytic one, depends on the difference in electrode potential of the two isotopes. They showed that if fine drops of lithium amalgam are allowed to fall through a solution of a lithium salt, the ratio of ${}^7\text{Li} : {}^6\text{Li}$ is not the same in the two phases, and ${}^6\text{Li}$ is carried preferentially by the amalgam. They carried out the process in a fractionation column consisting of a vertical glass tube 18 m. high and of 4 mm. internal diameter, which was filled with a solution of a lithium salt (the chloride in alcohol, or the bromide in alcohol-dioxan). Over half a ton of lithium amalgam (0.5–0.7 M with respect to lithium) was prepared, and in each experiment 10 litres of the amalgam were used in a 24-hour run, after which the material at the foot of the column was removed for analysis. In one of the best runs the atomic weight of the lithium in the salt from the foot of the column had been decreased from 6.940 to 6.855, i.e., an increase in the ratio of ${}^6\text{Li} : {}^7\text{Li}$ from 1 : 11.6 to 1 : 5.1 had been effected. This is an enrichment comparable with that of Holleck.

With lithium, therefore, quite considerable isotopic separations have been achieved by electrolytic and electrochemical methods, and this work may lead to further attempts with other elements. The fractional electrolysis of a solution of mercurous nitrate had been tried some years previously by J. Kendall,⁴⁴ who claimed to have obtained a very slight separation of the mercury isotopes, but the observed changes in density of the metal were disappointingly small.

(4) *Separation by Means of Fractional Distillation.*—One of the methods tried by Aston in his first attempts to separate the isotopes of neon was that of fractional distillation over charcoal cooled in

⁴² T. I. Taylor and H. C. Urey, *J. Chem. Physics*, 1938, **6**, 429.

⁴³ *J. Amer. Chem. Soc.*, 1936, **58**, 2519.

⁴⁴ *Ibid.*, 1933, **55**, 2612; see also ref. (37).

liquid air, but no measurable separation was achieved. The more successful attempts of W. H. Keesom and H. van Dijk⁴⁵ by rectification of neon at or near its triple point, which were recorded by Aston in his survey, have since been considerably improved upon. In a glass rectifying apparatus for the separation of relatively large quantities, fractions of atomic weight 20.091 and 20.574 (normal atomic weight, 20.183) have been obtained.⁴⁶ In later experiments⁴⁷ neon of atomic weight 21.157 was prepared. It may be recalled that H. C. Urey and his co-workers effected the first concentration of deuterium by the method of fractional distillation near the triple point. Small increases in the concentration of ^{18}O have been found in residues from the fractional distillation of liquid air and liquid oxygen.^{48, 49, 50}

In 1933 G. N. Lewis and R. E. Cornish⁵¹ announced that by means of fractional distillation they had produced small changes in the density of water due to separation of the isotopes of hydrogen and of oxygen. Since then several workers have tried to improve the fractional distillation method for the preparation of water which is denser than the normal owing to an increased concentration of the heavy isotopes of oxygen. Density increases due to concentration of deuterium must, of course, be eliminated or allowed for, as in the electrolytic production of "heavy" oxygen water. M. H. Wahl and H. C. Urey⁵² measured the relative vapour pressures of H_2^{16}O and H_2^{18}O by using a simple distillation process, in which case the ratio of the vapour pressures is equal to the simple-process fractionation factor q . They found that q decreases from 1.089 at 11.25° to 1.062 at 46.35° , giving an extrapolated value of 1.025 at 100° . Since these values differ only slightly from unity, efficient fractional distillation columns must be used in order to obtain a reasonable separation of the oxygen isotopes. The conditions necessary to obtain the best results, and the detailed working of a fractionating column, consisting of alternate stationary and rotating cones to provide a large surface, have been described by J. R. Huffman and H. C. Urey.⁵³ During the time their still was run it produced about 200 c.c. of water containing 0.85% of H_2^{18}O , and it is considered capable of producing water

⁴⁵ *Proc. K. Akad. Wetensch. Amsterdam*, 1931, **34**, 42.

⁴⁶ *Ibid.*, 1934, **37**, 615.

⁴⁷ *Ibid.*, 1935, **38**, 809.

⁴⁸ E. R. Smith, *J. Chem. Physics*, 1934, **2**, 298.

⁴⁹ R. Klar and A. Krauss, *Naturwiss.*, 1934, **22**, 119.

⁵⁰ D. F. Stedman, *Canadian J. Res.*, 1935, **13**, 114.

⁵¹ *J. Amer. Chem. Soc.*, 1933, **55**, 2616.

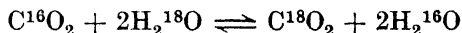
⁵² *J. Chem. Physics*, 1935, **3**, 411.

⁵³ *Ind. Eng. Chem.*, 1937, **29**, 531; see also G. B. Pegram, H. C. Urey, and J. R. Huffman, *Physical Rev.*, 1936, **49**, 883.

three times as concentrated. A still built by H. E. Watson ⁵⁴ has already given water with a total increased density of 700 parts per million (approximately half due to deuterium). D. F. Stedman ⁵⁰ has also recorded small separations of the oxygen isotopes by the distillation of water. Although the concentrations of heavy oxygen water obtained so far are not very large, they are sufficient for many purposes, such as the study of oxygen exchange reactions in solution, ⁵⁵ since measurements of the density of water can be carried out accurately to 1 part per million.

An attempt has also been made ⁵⁶ to concentrate ¹⁵N by the fractional distillation of liquid ammonia, but only slight separation has been effected in the preliminary experiments.

(5) *Separation by Chemical Exchange Methods.*—The marked differences in chemical properties of hydrogen and deuterium compounds are now well known. Equilibrium constants involving hydrogen and deuterium, calculated from statistical theory using spectroscopic data, have in many cases been confirmed by experiment and have formed the basis of methods for separating the two isotopes. In recent years, heterogeneous equilibria in exchange reactions involving isotopes of elements other than hydrogen have been used to effect isotopic separations. H. C. Urey and L. J. Greiff ⁵ showed theoretically that slight differences in the chemical properties of isotopic compounds of the lighter elements should exist, and calculated the separation factors of several exchange reactions. For example, the equilibrium between liquid water and gaseous carbon dioxide



gives a separation factor of 1.047 at 0°, and favours the concentration of ¹⁸O in the carbon dioxide. This was confirmed experimentally by L. A. Webster, M. H. Wahl, and H. C. Urey. ⁵⁷ In most of the other examples given by Urey and Greiff the theoretical separation factors are also small, and the separation that can be expected in a simple-process equilibrium of this type is very slight. To effect reasonable separations, the exchange of isotopes between the liquid and the gas phase must be allowed to proceed continuously in a fractionating column in which counterflow of liquid and gas is maintained. The principles and technique of chemical exchange separations are therefore essentially the same as those of fractional distillation. The process consists in the flow of liquid phase downward through a column of high efficiency, at the bottom of which

⁵⁴ Cf. S. C. Datta, J. N. E. Day, and C. K. Ingold, *J.*, 1937, 1969.

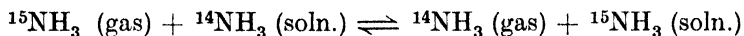
⁵⁵ See, e.g., ref. (54).

⁵⁶ M. H. Wahl, J. R. Huffman, and J. A. Hipple, *J. Chem. Physics*, 1935, 3, 434.

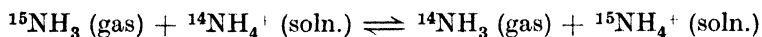
⁵⁷ *Ibid.*, p. 129.

the gas from the liquid phase is liberated by boiling and returned upward through the column.

Preliminary experiments by H. C. Urey and his co-workers⁵⁸ demonstrated the usefulness of chemical exchange methods for concentrating the isotopes ^{15}N and ^{13}C , and improved separations have since been obtained. Using the 35 ft. column originally devised for the fractional distillation of water,⁵³ H. C. Urey, M. Fox, J. R. Huffman, and H. G. Thode⁵⁹ have studied the exchange reactions



with aqueous and alcoholic solutions, and



with solutions of the nitrate and sulphate. The two most successful runs yielded 61 g. of ammonium chloride in which the nitrogen contained 2.5% of ^{15}N (*i.e.*, a 6.5-fold increase), and larger amounts of not quite so concentrated material. By means of the exchange reaction between ammonia and ammonium nitrate, using an arrangement of two distillation columns in cascade, a 46-fold increase in ^{15}N has now been effected and a sample containing 14.5% of heavy nitrogen obtained.⁶⁰ A column has also been designed to give a production of 1.5 g. of ^{15}N per 24 hours in concentrations of about 60%. In the same paper a 3-fold increase in the concentration of ^{34}S in a solution of sodium hydrogen sulphate by exchange reaction with sulphur dioxide has been recorded, and further concentrations are foreshadowed.

An interesting application of chemical exchange methods in a liquid-solid system has been used by T. I. Taylor and H. C. Urey^{40, 42} to effect a partial separation of the isotopes of alkali metals. This depends on the fact that when a complex hydrated aluminosilicate of the zeolite type is shaken with a solution containing an alkali-metal ion, an exchange of the positive ion takes place, and partial replacement occurs according to the equilibrium $\text{A}^+ + \text{BZ} \rightleftharpoons \text{B}^+ + \text{AZ}$. Taylor and Urey assumed that with a mixture of two isotopes, *e.g.*, ^6Li and ^7Li , one isotope would be taken up more readily than the other. The fractionation factor for a single process is then given by the distribution of the two isotopes between the two phases, *viz.*, $q = (^6\text{LiZ}/^7\text{LiZ})/(^6\text{Li}^+/^7\text{Li}^+)$. The value of q , however, is only slightly greater than unity, as in most isotopic exchange reactions, and so the separation effect is multiplied by using long

⁵⁸ H. C. Urey and A. H. W. Aten, *Physical Rev.*, 1936, **50**, 575; H. C. Urey, A. H. W. Aten, and A. S. Keston, *J. Chem. Physics*, 1936, **4**, 622.

⁵⁹ *J. Amer. Chem. Soc.*, 1937, **59**, 1407; see also ref. (6).

⁶⁰ H. G. Thode, J. E. Gorham, and H. C. Urey, *J. Chem. Physics*, 1938, **6**, 296.

columns of zeolite, about 30—100 feet long. If a solution of lithium chloride is added at the top of such a column originally filled with a sodium zeolite and distilled water, all the way down the column one lithium isotope is held back more than the other, and the first lithium chloride coming through at the bottom should have a changed isotope ratio. This is called the leading sample. After the column has been converted into a lithium zeolite, a solution of sodium chloride is passed through it. One lithium isotope is replaced more readily than the other by the sodium ion, and the last lithium chloride coming through, called the tailing sample, should have the isotope ratio changed in the opposite direction to that of the leading sample. In other experiments the procedure was somewhat modified by using the principles of chromatographic analysis. Taylor and Urey found that the normal ratio of ${}^7\text{Li} : {}^6\text{Li}$ of 11.7 : 1 (determined mass-spectrographically) was increased to 12.3—13.3 : 1 in the leading samples and decreased to 8.8—8.9 : 1 in the tailing samples. This means that ${}^6\text{Li}^+$ is preferentially taken up by the zeolite, and is not so readily removed as ${}^7\text{Li}^+$. Further experiments on the influence of the solvent and of the specific nature of the zeolite are being made.

The same general procedures were also tried for potassium and for the nitrogen isotopes in the ammonium ion. In both cases small changes in the isotope ratio were observed, but in a direction opposite to that found with lithium, *i.e.*, the heavier isotope was more readily taken up by the zeolite. This suggests that the process responsible for the fractionation is essentially an equilibrium one rather than one due to differences in the rate of diffusion or reaction, since, otherwise, the light isotopes would all diffuse faster, resulting in changes of the isotopic ratio in the same direction.

Other chemical methods have been used to obtain small separations of isotopes. For example, H. S. Taylor and A. J. Gould⁶¹ obtained a partial separation of the oxygen isotopes in the decomposition of 30% hydrogen peroxide in presence of colloidal platinum. Slight fractionation of the isotopes of oxygen, chlorine, bromine, and nitrogen in chemical reactions have been reported by E. Ogawa,⁶² and R. S. Bradley⁶³ observed a small chemical separation of the chlorine isotopes when carbon tetrachloride was heated with sodium amalgam. The reaction $4\text{Na} + \text{CCl}_4 = \text{C} + 4\text{NaCl}$ occurs almost quantitatively, and the ${}^{35}\text{Cl}$ reacts preferentially to ${}^{37}\text{Cl}$.

(6) *Separation by Photochemical Methods.*—These have not received much further study, and brief mention will be made only of

⁶¹ *J. Amer. Chem. Soc.*, 1934, **56**, 1823.

⁶² *Bull. Chem. Soc. Japan*, 1936, **11**, 428.

⁶³ *Nature*, 1936, **137**, 403.

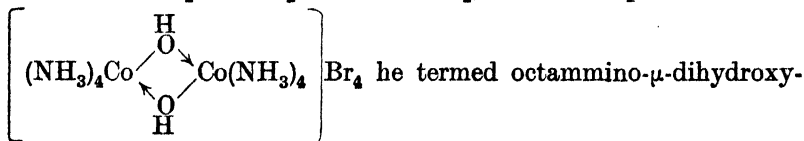
two other papers in which the separation of isotopes by photochemical means has been reported since the publication of Aston's survey. W. Kuhn and H. Martin ⁶⁴ have published a more detailed account of their method, which resulted in a partial separation of the isotopes of chlorine. A photochemical method has also been used by K. Zuber ⁶⁵ to effect a partial separation of ²⁰⁰Hg and ²⁰²Hg by selective irradiation of ordinary mercury vapour with two components of the mercury resonance line at 2537 Å.

In the experiments carried out so far on the separation of isotopes, only about 16 elements have been used. An examination of the International Table of stable isotopes for 1938 ⁶⁶ shows that, of the elements from hydrogen to bismuth in the Periodic Table, about 20 are simple, *i.e.*, are represented by only one mass number. The remaining elements are complex and consist of from 2 to 10 isotopes, the lighter elements usually having not more than 2 or 3 isotopes. With the doubtful exception of the mass number 5, which may belong to an isotope of lithium, all the mass numbers from 1 to 209 have been appropriated by known stable isotopes. Some mass numbers are represented more than once, owing to the existence of isobares, and in the 1938 table about 270 different kinds of atom are included in the above range of mass number. It is obvious, therefore, that in the attempts to separate the isotopes of individual elements there is still a very large field for experiment, and no doubt further advances will be made during the next few years.

O. J. W.

4. POLYNUCLEAR METALLIC COMPOUNDS.

Our knowledge of polynuclear metallic compounds is at present confined largely to compounds in which the metallic atoms show a covalency of 4 or of 6. Werner investigated the 6-covalent metallic compounds in some detail, and showed that the two (or more) octahedra could be linked through one, two, or three "bridging" groups. The chief bridging groups known to Werner were: -OH, -O-, -O₂-, -NH₂, -NH-, -NO₂, and a compound such as



he termed octammino- μ -dihydroxy-

⁶⁴ *Z. physikal. Chem.*, 1933, **B**, **21**, 93.

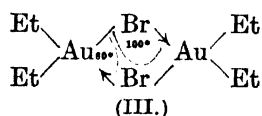
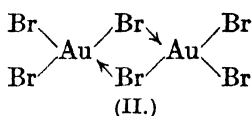
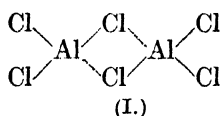
⁶⁵ *Nature*, 1935, **136**, 796.

⁶⁶ O. Hahn, *Ber.*, 1938, **71**, 1; also *Union Internat. Chim.*, 1938, pp. 3-14.

groups. The study of similar derivatives of 4-covalent metals had been largely neglected until recently, and this Report is confined therefore mainly to the considerable progress which has been achieved in the elucidation of the structure of the polynuclear 4-covalent metallic compounds during the last few years.

Since 1857, when H. St. C. Deville and L. Troost ¹ showed that the vapour densities of aluminium and ferric chlorides corresponded to Al_2Cl_6 and Fe_2Cl_6 respectively, it has been recognised that molecules of certain metallic chlorides can unite in pairs, and P. Pfeiffer ² first suggested the structure (I) for aluminium chloride. Decisive evidence for this bridged structure has now been obtained for derivatives of gold, palladium, aluminium, cadmium, and mercury, and considerable evidence has also been obtained for derivatives of platinum, zinc, copper, and silver. These metals will be discussed in turn.

Gold.—The vapour density of auric chloride between 150° and 260° has been shown by W. Fischer ³ to correspond to the



bimolecular form Au_2Cl_6 , and the molecular weight of auric bromide in boiling bromine has been shown by A. Burawoy and C. S. Gibson ⁴ to correspond similarly to Au_2Br_6 , which is formulated as (II). "Diethylmonobromogold," originally prepared by C. S. Gibson and W. J. Pope, ⁵ has been shown by Gibson and his co-workers ⁶ to have a molecular weight corresponding to $[\text{Et}_2\text{AuBr}]_2$ in benzene and bromoform, and the bridged structure (III) was therefore allotted to this compound. This structure for the crystalline compound was decisively proved by X-ray analysis, ⁷ which showed that the molecule was planar and that the intervalency angles in the ring were those shown in (III). The compound should therefore be termed tetraethyl- μ -dibromodigold. "Monoethyldibromogold" ⁸ also showed in bromoform solution a molecular weight corresponding to $[\text{EtAuBr}_2]_2$ and was therefore formulated as the unsymmetrical (IVa) and the symmetrical form (IVb), the latter being theoretically capable of *cis-trans*-isomerism. Only one form was actually isolated, however. "Di-*n*-propylcyanogold" proved to have the molecular formula $[\text{Pr}_2\text{AuCN}]_4$, and the structure (V) having a

¹ *Compt. rend.*, 1857, **45**, 821.

² Werner-Pfeiffer, "Neuere Anschauungen auf dem Gebiete der Anorganischen Chemie," 5th Edition, 1923, p. 285.

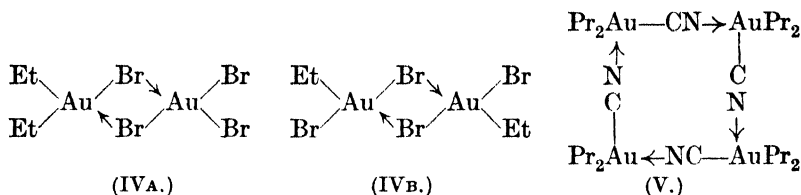
³ *Z. anorg. Chem.*, 1929, **184**, 333.

⁴ *J.*, 1907, **91**, 2061.

⁵ *J.*, 1935, 217.

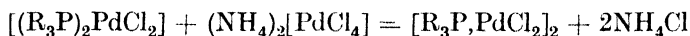
⁶ *J.*, 1930, 2531; 1934, 860.

planar 12-membered ring was allotted to it.⁷ Decisive evidence for the structures (IV) and (V) has not yet appeared.

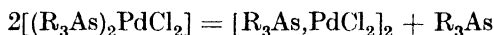


Palladium and Platinum.—It has been known for many years that platinum, when heated with phosphorus pentachloride, gave two compounds of composition $[(\text{PCl}_3)_2\text{PtCl}_2]$ and $[(\text{PCl}_3)_3\text{PtCl}_2]$. These reacted with alcohols (ROH) to give the corresponding ester derivatives, whose molecular formulæ were shown to be $[\{\text{P}(\text{OR})_3\}_2\text{PtCl}_2]$ and $[\{\text{P}(\text{OR})_3\}\text{PtCl}_2]_2$, respectively. Palladium gave analogous derivatives.

F. G. Mann and D. Purdie⁸ have prepared similar "bimolecular" compounds of aliphatic tertiary phosphines and arsines by the interaction of the corresponding dichlorobisphosphine(or arsine)-palladium and ammonium palladochloride in alcoholic solution :

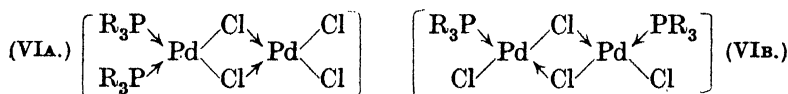


The arsine compounds were also prepared by thermal decomposition :



a method which cannot be employed for the phosphine derivatives, since the compounds $[(\text{R}_3\text{P})_2\text{PdCl}_2]$ distil unchanged on heating. The phosphine- and arsine-dipalladium compounds so obtained crystallise readily from many organic solvents and usually have sharp m. p.'s, and the first detailed study of the structure and reactions of a series of bridged dimetallic compounds has thus been possible.

These bridged phosphine and arsine compounds can theoretically exist in the unsymmetrical (VI A) and in the *cis*- and *trans*-symmetrical (VI, B and C) forms. In the crystalline state only one form

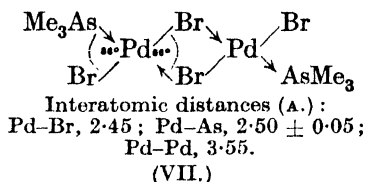
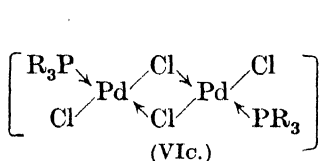


occurs: since, however, the crystalline *n*-propyl (and the *n*-butyl) phosphine and arsine derivatives are isomorphous, corresponding

⁷ A. Burawoy, C. S. Gibson, G. S. Hampson, and H. M. Powell, *J.*, 1937, 1690.

⁸ *J.*, 1936, 873.

phosphine and arsine compounds must have the same structure, and differences in reaction must therefore be due essentially to differences



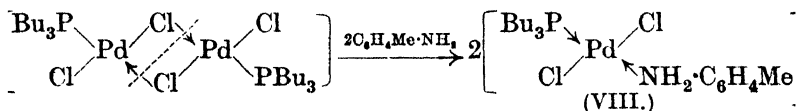
in stability. Similar bridged compounds containing the bromine, iodine, nitro-, and thiocyanato-radicals have also been prepared.

A detailed crystallographic examination proved that the isomorphous trimethylarsine tetrachloro- and tetrabromo-compounds, $[(\text{Me}_3\text{As})_2\text{Pd}_2\text{X}_4]$, possessed planar molecules of the *trans*-symmetrical type, the dimensions of the tetrabromo-molecule being shown in (VII).⁹

There is evidence, both physical and chemical, however, that these dipalladium compounds, although crystallising in only one form, give in organic solvents a tautomeric mixture of the three possible forms (VI; A, B, and C). A. E. Finn⁸ has found the dipole moment of the *n*-butylphosphine derivative, $[(\text{Bu}_3\text{P})_2\text{Pd}_2\text{Cl}_4]$, in benzene at 25° to be 2.34 D., and that of the arsine derivative, $[(\text{Bu}_3\text{As})_2\text{Pd}_2\text{Cl}_4]$, to be 2.52 D. The expected moments, if these compounds existed in each of the three forms, would be, for the unsymmetrical form (VIA), 12–14; for the *cis*-symmetrical (VIB), 7–8; for the *trans*-symmetrical (VIC), 0. The experimental values indicate therefore a mixture either of (VIB) and (VIC), or of all three forms.

The chemical evidence for the existence of the symmetrical forms (VI, B and C) in solution is summarised under two headings:

(i) The butylphosphine (or arsine) compound, when treated in cold solution with two equivalents of a monoacid base, *e.g.*, *p*-toluidine, gives solely two molecules of the very soluble compound

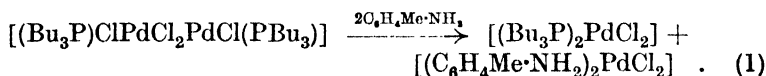


(VIII), the bridged ring splitting diagonally as shown. The same product would clearly be given by the *cis*-symmetrical form (VIB), since in unbridged non-chelated palladium compounds such as (VIII), the interconversion *cis* \rightleftharpoons *trans* occurs at room temperature, the more stable *trans*-form being usually the sole final product.¹⁰

⁹ F. G. Mann and A. F. Wells, *J.*, 1938, 702; A. F. Wells, *Proc. Roy. Soc.*, 1938, A, 167, 169.

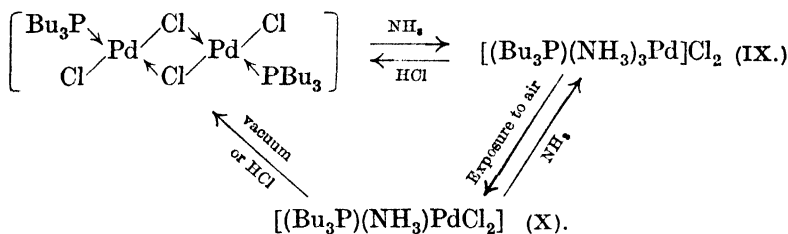
¹⁰ F. G. Mann, D. Crowfoot, D. C. Gattiker, and N. Wooster, *J.*, 1935, 1642.

The tetranitro-compound, $[(\text{Bu}_3\text{P})_2\text{Pd}_2(\text{NO}_2)_4]$, similarly gives $[(\text{Bu}_3\text{P})(\text{C}_6\text{H}_4\text{Me}\cdot\text{NH}_2)\text{Pd}(\text{NO}_2)_2]$, and in both reactions the *p*-toluidine may be replaced by aniline, pyridine, or quinoline. In view of the evidence given below for the facile interchange of groups, both bridged and unbridged, in the dipalladium compounds, this reaction with *p*-toluidine has a further significance, in that it shows that the scission of the bridged compounds must be severely controlled by specific factors: if the groups concerned were entirely free for mutual rearrangement, the reaction would proceed as in equation (1), since the second of these dichloro-compounds is almost



insoluble in the usual solvents employed.

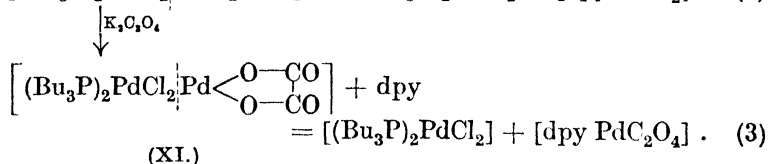
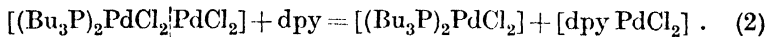
(ii) The butylphosphine tetrachloro-compound gives a similar reaction with ammonia, but all the chlorine is evicted from the complex, giving the triammino-compound (IX), a reaction which is readily reversed by hydrochloric acid. The compound (IX) is



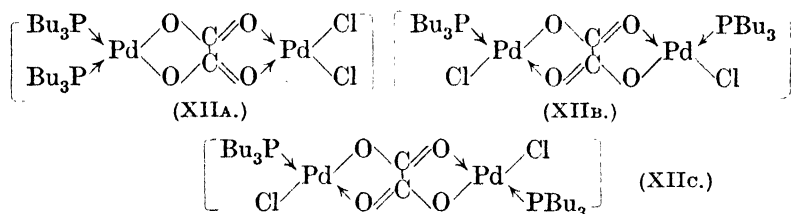
unstable on prolonged exposure to air, losing two molecules of ammonia and giving the non-ionic monoammino-compound (X), which in turn, under the influence of a vacuum or of hydrochloric acid, readily regenerates the original bridged tetrachloro-compound.

The chemical evidence originally adduced by Mann and Purdie for the existence of the unsymmetrical form (VIa) was based partly on two reactions. When the butylphosphine tetrachloro-compound was treated in solution with one equivalent of $\alpha\alpha'$ -dipyridyl, it appeared to undergo a simple "vertical splitting" (2). Furthermore, the tetrachloro-compound when treated with potassium oxalate gave the bridged dichloro-oxalate (XI), in which the oxalate group in accordance with previous experience was considered to be chelated to one palladium atom by the normal operation of two covalencies, thus necessitating the unsymmetrical structure. This structure was apparently confirmed by the fact that the dichloro-oxalate gave a similar reaction with dipyridyl (3), the

unbridged dichloride and mono-oxalate being formed. Precisely parallel reactions were given also by the butylphosphine tetranitro-compound. The dipole moment of the dichloro-oxalate was found, however, by Finn ⁸ to be 3.55 D., whereas the structure (XI) would

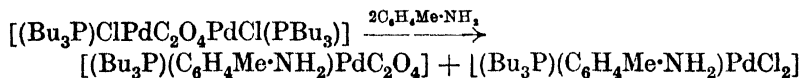


require a moment of 12–14 D. Hence Finn suggested that the oxalate group bridged the palladium atoms in the dichloro-oxalate, which could therefore exist theoretically in the unsymmetrical form (XIIA) and in the *cis*- and *trans*-symmetrical forms (XII, B and C). A tautomeric mixture of these three forms would explain



the observed moment. The dichloro-oxalate has therefore been further investigated by J. Chatt, F. G. Mann, and A. F. Wells,¹¹ who find that the Pd–Pd distance in this compound is 5.48 Å. Now when the palladium atoms are bridged by chlorine atoms,⁹ the Pd–Pd distance is known to be *ca.* 3.4 Å.; if, however, the palladium atoms are bridged by an oxalate group, the calculated Pd–Pd distance is *ca.* 5.3 Å. Furthermore, the crystallographic evidence shows almost certainly that the molecule has a centre of symmetry. The oxalate group therefore must bridge the palladium atoms, and the molecule in the crystal probably has the *trans*-symmetrical structure (XIIc).

In addition, the dichloro-oxalate reacts with two equivalents of *p*-toluidine thus:

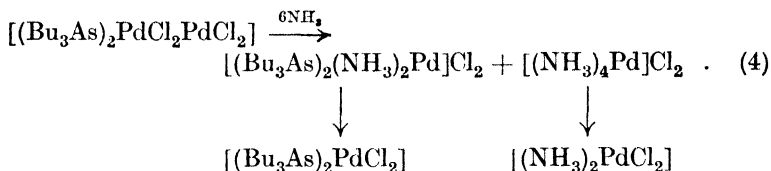


The interpretation of this reaction is very difficult on the basis of structure (XI), but relatively simple on that of (XIIc). It is clear, however, from the structure of the dichloro-oxalate that the action

of dipyridyl cannot be the simple "vertical splitting" shown in (2) and (3), and that these reactions cannot be cited as evidence for the unsymmetrical structure (VIa). The probable mechanism of the action of dipyridyl and of *p*-toluidine is discussed by these authors.

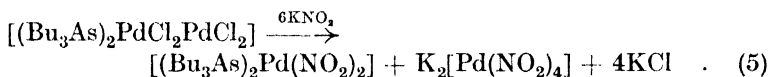
The chief chemical evidence ⁸ for the unsymmetrical structure is therefore the following :

(i) The butylarsine tetrachloro-compound (isomorphous with the butylphosphine derivative), when cautiously treated with ammonia,

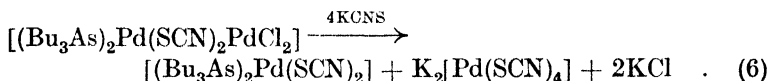


reacts as in (4). Both products on exposure to air lose two molecules of ammonia as shown.

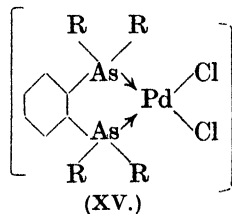
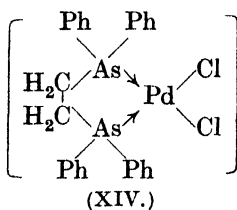
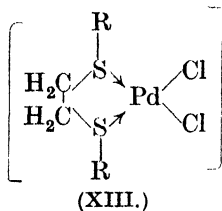
(ii) The same compound readily reacts with excess potassium nitrite, giving $[(\text{Bu}_3\text{As})_2\text{Pd}(\text{NO}_2)_2]$:



(iii) The corresponding dichloro-dithiocyanate, in which the -SCN groups are known to bridge the palladium atoms, reacts with excess potassium thiocyanate to give $[(\text{Bu}_3\text{As})_2\text{Pd}(\text{SCN})_2]$:



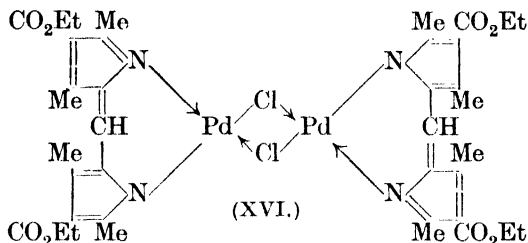
In an attempt to synthesise a bridged compound which must necessarily have the unsymmetrical structure, J. Chatt and F. G. Mann ¹² have prepared the disulphide compound (XIII), in which R = Et and also *n*-octyl, the diarsine compound (XIV), and also the compound (XV), in which R = Me and also *n*-butyl. If these



chelated compounds reacted with ammonium palladochloride, the bridged compounds so formed must have the unsymmetrical

¹² *Nature*, 1938, **142**, 709.

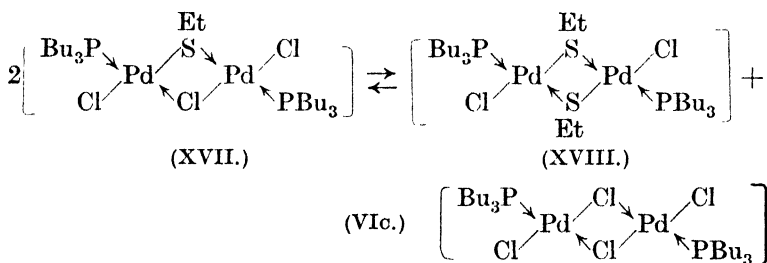
structure; actually, however, none of these compounds would form bridged derivatives. This inability cannot be due to the chelated ring as such, since several chelated-ring, bridged dipalladium compounds are known (*e.g.*, XVI¹³), in all of which, however, the



chelated ring is joined to the metal by *one co-ordinate and one covalent link*, and the symmetrical structure is thus possible.

The three reactions given above provide very strong *prima facie* evidence for the unsymmetrical structure of the tetrachloro-compound. The failure to isolate a compound which must necessarily have the unsymmetrical bridged structure raises doubt, however, as to whether compounds possessing this structure are sufficiently stable to exist other than in solution, and then only in tautomeric equilibrium with the symmetrical forms. Alternatively, the three reactions may be more complex than the equations indicate, and may not therefore provide the required evidence.

The remarkable mobility of the constituent groups in these bridged palladium compounds has recently been demonstrated by J. Chatt and F. G. Mann,¹⁴ who, by treating the butylphosphine



tetrachloro-compound with ethylthiol, have prepared the compounds $[(\text{Bu}_3\text{P})_2\text{Pd}_2\text{Cl}_3(\text{SEt})]$ and $[(\text{Bu}_3\text{P})_2\text{Pd}_2\text{Cl}_2(\text{SEt})_2]$. The latter does not react with dipyridyl or *p*-toluidine, and therefore cannot possess the PdCl_2Pd ring, *i.e.*, the $-\text{SEt}$ radicals bridge the palladium atoms and the compound has the structure (XVIII). The mono-ethylthiol compound (XVII) in solution gives an equilibrium mixture

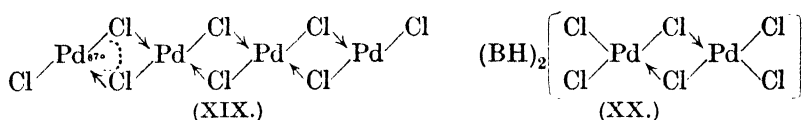
¹³ C. R. Porter, *J.*, 1938, 368; see also Section 5 of this Report, p. 164.

¹⁴ *J.*, 1938, 1949.

of the bisethylthiol compound (XVIII) and the original tetrachloro-compound (VIc). This is shown by considerable physical and chemical evidence: for example, when solutions of the bis-thiol compound (XVIII) and the tetrachloro-compound (VIc) are mixed, the least soluble monothiol compound (XVII) crystallises out. Chemical reagents, however, shift the equilibrium point to the right, the monothiol compound (XVII) in solution reacting as a mixture of (XVIII) and (VIc).

It is probable that the labile nature of the groups in these bridged dipalladium compounds is not a specific property of the bridged structure as such, but is due primarily to the loose co-ordination of groups in complex palladium compounds generally.

A detailed crystallographic investigation of palladium dichloride has recently been made by A. F. Wells,¹⁵ who found it to consist of long chains of palladium atoms bridged by chlorine atoms (XIX), the Cl-Pd-Cl angle within the ring so formed being 87°. The



fact that the corresponding angle in the bridged trimethylarsine compound (VII) is 86° confirms the essential identity of the ring structure in the two compounds, and the PdCl_2 units in (XIX) are doubtless united through a series of co-ordinate links as shown, although, of course, when once the chain is formed there is no essential difference between the links involved.

The above work on bridged compounds elucidates the probable constitution of many palladium and platinum compounds to which unlikely structures have been attributed by past workers. For instance, A. Gutbier and C. Fellner¹⁶ have described several salts of amine hydrochlorides with palladium dichloride, to which they assigned the general formula $\text{B}_n\text{H}[\text{PdCl}_3]_n$. It is almost certain that these compounds have the double formula $(\text{BH})_2[\text{Pd}_2\text{Cl}_6]$ and the structure (XX), in which the anion contains two palladium atoms bridged through chlorine atoms. The formation of this $[\text{Pd}_2\text{Cl}_6]$ ion enables each palladium atom to acquire the desired six electrons (precisely as in the above bridged phosphine and arsine compounds), and hence the bridging process presumably stops at this stage. In crystalline palladium dichloride (XIX), the bridging process gives six electrons to each palladium atom with the exception of the terminal metallic atoms, which acquire only four electrons. This deficiency of electrons on the terminal palladium atoms is thus probably intimately

¹⁵ *Z. Krist.*, 1938, **100**, 189.

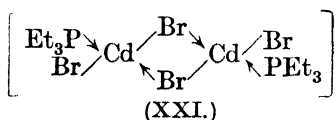
¹⁶ *Z. anorg. Chem.*, 1916, **95**, 169.

associated with the indefinite length of the bridged chain. Several other palladium and platinum compounds, which past investigators have formulated as containing either direct metal-to-metal links or alternatively 5-covalent metallic atoms, are discussed by F. G. Mann and D. Purdie,⁸ and their probable bridged structure indicated.

Aluminium.—Decisive evidence¹⁷ has only recently been obtained (by electron diffraction methods) that aluminium chloride, bromide, and iodide have the bridged structure (I), the 4-covalent aluminium complex being tetrahedral, and the unbridged halogen atoms being therefore in a plane at right angles to that of the ring.

Cadmium, Zinc, and Mercury.—G. J. Burrows¹⁸ and his co-workers have briefly described two types of complex compound which phenyldimethylarsine gives with cadmium, zinc, and mercuric halides. The first is given the formula $(\text{PhMe}_2\text{As})_2\text{MX}_2$, where $\text{M} = \text{Cd}, \text{Zn}$ or Hg , and $\text{X} = \text{halogen}$, and the second the formula $(\text{PhMe}_2\text{As})\text{MX}_2$. Although no molecular-weight determinations are recorded, the second type of compound undoubtedly has the bridged formulation (as VI), but owing to the tetrahedral disposition of these metallic atoms, the four terminal unbridged groups will lie in a plane at right angles to that of the bridged ring, as in aluminium chloride.

The structure and reactions of the compounds which the lower trialkyl-phosphines and -arsines give with the above metallic halides are being examined in detail in the Cambridge laboratories. Cadmium bromide is found to give three distinct derivatives: (i) The



normal unbridged tetrahedral compound $[(\text{R}_3\text{P})_2\text{CdBr}_2]$. (ii) The bridged compound $[(\text{R}_3\text{P})_2\text{Cd}_2\text{Br}_4]$; this should exist in three forms similar to (VIA, B, and c), but crystallo-

graphic evidence shows that the ethyl compound has the *trans*-symmetrical structure (XXI). (iii) A compound of composition $(\text{R}_3\text{P})_3(\text{CdBr}_2)_2$; crystal analysis indicates that this "sesqui" product is a new type of complex compound, and not a lattice combination of two molecules of (i) with one of (ii).

Mercuric halides also give phosphine compounds of types (ii) and (iii). The bridged derivative $[(\text{Pr}^n_3\text{P})_2\text{Hg}_2\text{Br}_4]$ possesses a centre of symmetry and therefore also has the *trans*-symmetrical structure (as XXI). The iodide, $[(\text{Pr}^n_3\text{P})_2\text{Hg}_2\text{I}_4]$, occurs in two crystalline forms⁹ of correct molecular weight, one colourless and the other yellow, but it is not yet certain whether they are isomeric forms or merely dimorphic forms of the same substance. Bridged

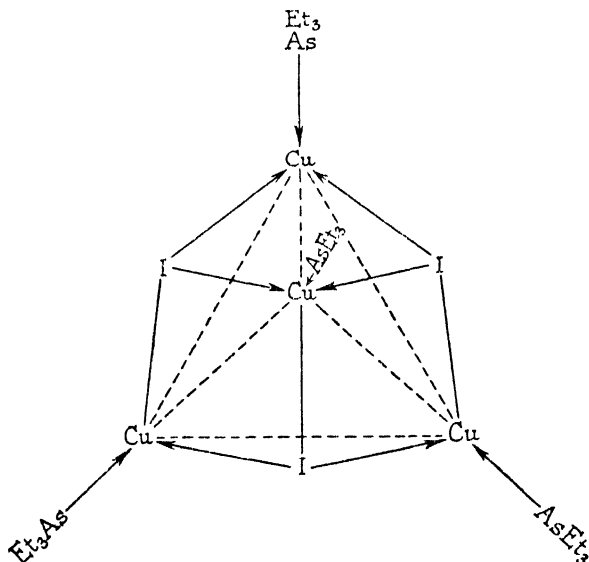
¹⁷ K. S. Palmer and N. Elliott, *J. Amer. Chem. Soc.*, 1938, **60**, 1852.

¹⁸ *J. Proc. Roy. Soc. N.S.W.*, 1936, **70**, 62, 218, 222.

“mixed-metal” compounds, *e.g.*, $[(Pr^a_3P)BrCdBr_2HgBr(Pr^a_3P)]$, have also been prepared and are under examination.

Copper and Silver.—Four-covalent copper appears to form at least three types of polynuclear compound.

(i) The addition products of the lower trialkyl-phosphines and -arsines with the cuprous halides, previously considered to be $[R_3P(As) \rightarrow CuX]$, have now been shown by Mann, Purdie, and Wells¹⁹ to have a fourfold molecule, the ethylarsine-cuprous iodide



(XXII.) *Tetrakis(monoiodotriethylarsinecopper).*

The broken lines represent the edges of the tetrahedron formed by the four copper atoms, the apex occupied by the central copper atom being tilted **forward** to show all the four bonds joined to this atom. The iodine atom behind the rear face of the tetrahedron is not shown. The unbroken lines without barbs represent covalent links, those with barbs co-ordinate links.

derivative thus being $[Et_3As \rightarrow CuI]_4$. Crystallographic analysis of this compound showed that the four copper atoms occupy the apices of a regular tetrahedron (XXII); the iodine atoms are situated each above the central point of one face of this tetrahedron, so that they also form a tetrahedron external to that of the copper atoms. Beyond each copper atom is an arsenic atom lying on the elongation of the axis joining the centre of the inner tetrahedron to the copper atom. The iodine atoms have thus become 3-covalent, being joined to the three neighbouring copper atoms by one covalent and two co-ordinate links. The formation of the fourfold molecule

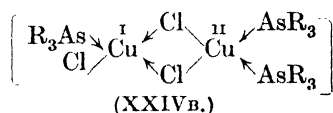
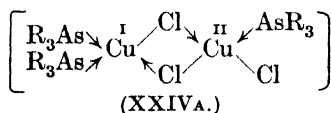
¹⁹ *J.*, 1936, 1503.

has thus enabled each of the tetrahedral 4-covalent cuprous atoms to become joined by a covalent link to one iodine and by co-ordinate links to one arsenic and two iodine atoms, and thus by acquiring seven electrons to attain the electronic structure of krypton. The crystallographic evidence also shows, not only that the 4-covalent arsenic atom is tetrahedral, but also that the 3-covalent iodine atom can be regarded as being at the apex of a tetrahedron with its valencies directed to the remaining three apices, and in this respect resembles 3-covalent sulphur.

It is noteworthy, however, that G. J. Burrows and E. P. Sanford²⁰ have shown that the molecular weights of certain cuprous derivatives of phenyldimethylarsine, *e.g.*, $[\text{PhMe}_2\text{As} \rightarrow \text{CuI}]$, indicate decisively that these compounds have the "unimolecular" formula.

(ii) There is little doubt that the cuprous compounds of empirical composition dpy CuI ¹⁹ and $(\text{PhMe}_2\text{As})_2\text{CuI}$ ²⁰ have the doubled bridged constitution (as XXIII), but indifferent crystalline form or instability has so far hindered investigation.

(iii) D. P. Mellor, G. J. Burrows, and B. S. Morris²¹ have described two compounds of formula $(\text{PhMe}_2\text{As})_3\text{Cu}_2\text{Cl}_3$, obtained by the



action of the arsine on cupric chloride. The two forms are blue and brown, severally, and give satisfactory molecular weights in nitrobenzene solution. The authors consider that part of the copper has undergone reduction to the cuprous state by the excess of arsine, and that isomeric bridged compounds are thus formed (XXIV, A and B), both containing a tetrahedral cuprous and a uniplanar cupric complex. These formulæ satisfy the necessary stereochemical and electronic conditions, and decisive evidence for the structure of the compounds would therefore be of great interest.

Trialkyl-phosphines and -arsines also combine with silver iodide²² to give fourfold molecules, and since $[\text{Pr}_3\text{As} \rightarrow \text{AgI}]_4$ is strictly isomorphous with $[\text{Et}_3\text{As} \rightarrow \text{CuI}]_4$, the silver compounds have a structure identical with (XXII), and the silver atoms thus attain the electronic state of xenon. Aurous halides, however, give only "unimolecular" compounds, $[\text{R}_3\text{P}(\text{As}) \rightarrow \text{AuX}]$, and the gold

²⁰ *J. Proc. Roy. Soc. N.S.W.*, 1936, **69**, 182.

²¹ *Nature*, 1938, **141**, 414.

²² F. G. Mann, A. F. Wells, and D. Purdie, *J.*, 1937, 1828.

atoms do not attempt to reach the electronic structure of radon. G. J. Burrows and R. H. Parker²³ have described some addition products of phenyldimethyl- and diphenylmethyl-arsine with silver salts, to which they assign ionic formulæ such as $[(\text{PhMe}_2\text{As})_2\text{Ag}]\text{Cl}$ and $[(\text{Ph}_2\text{MeAs})_2\text{Ag}]\text{NO}_3$. Since some of these compounds are freely soluble in organic solvents, such formulæ are unlikely, and it is more probable that they are bridged compounds $[(\text{R}_3\text{As})_2\text{AgCl}]_2$ similar in type to (VIc).

F. G. M.

5. CO-ORDINATION COMPOUNDS.

It will cause no surprise that the study of co-ordination compounds continues to be prosecuted with unabated vigour, when it is realised how far the co-ordination theory, in its modern form, has become interwoven into the fabric of chemistry. It would be impossible to survey co-ordination compounds on such a broad basis; accordingly, the scope of the present Report has been restricted to complex metallic compounds generally, as has been the practice formerly.¹ The main trend of investigation has continued to centre round the determination of the structure of co-ordination compounds with all the powerful physical methods at the disposal of the modern chemist—a refurbishing of old observations in the light of present-day knowledge.

It is only within the last few years that the amminated derivatives of ruthenium have been the subject of a comprehensive study. Some preliminary investigations have already been reported,² and these have been followed by some ten memoirs by K. Gleu and his co-workers³ on the ruthenium amines. It is found that the action of ammonia on ruthenium trichloride leads to the colourless crystalline hexammine $[\text{Ru},6\text{NH}_3]\text{Cl}_3$, from which a number of salts containing the anion $[\text{Ru},6\text{NH}_3]^{+++}$ can be prepared by double decomposition. With boiling concentrated hydrochloric acid, the foregoing hexammines furnish yellow, sparingly soluble $[\text{RuCl},5\text{NH}_3]\text{Cl}_2$. With aqueous ammonia, followed by ammonium dithionate, this pentammine gives $[\text{RuOH}(\text{NH}_3)_5]\text{S}_2\text{O}_8$ in colourless, sparingly soluble crystals which are changed into the aquo-pentammine $[\text{Ru}(\text{NH}_3)_5\text{H}_2\text{O}]_2(\text{S}_2\text{O}_8)_3 \cdot 2\text{H}_2\text{O}$ by aqueous dithionic

²³ *J. Amer. Chem. Soc.*, 1933, **55**, 4133.

¹ *Ann Reports*, 1936, **33**, 157.

² *Ibid.*, p. 171.

³ K. Gleu and K. Rehm, *Z. anorg. Chem.*, 1936, **227**, 237; K. Gleu, W. Breuel, and K. Rehm, *ibid.*, 1938, **235**, 201; K. Gleu and W. Breuel, *ibid.*, p. 211; K. Gleu and K. Rehm, *ibid.*, p. 352; K. Gleu, W. Cuntze, and K. Rehm, *ibid.*, 1938, **237**, 89; K. Gleu and W. Cuntze, *ibid.*, p. 187; K. Gleu and W. Breuel, *ibid.*, pp. 197, 326, 335, 350.

acid. The chloropentammine $[\text{RuCl}(\text{NH}_3)_5]\text{Cl}_2$ also forms the starting point for a series of tetrammines, since it reacts with sodium bisulphite with formation of $\text{Na}_4[\text{Ru}(\text{SO}_3\text{H})_2(\text{NH}_3)_2(\text{SO}_3)_2]\cdot 6\text{H}_2\text{O}$ and $[\text{Ru}(\text{SO}_3\text{H})_2(\text{NH}_3)_4]$. The latter sulphite is acidic and affords an ammonium salt $(\text{NH}_4)_2[\text{Ru}(\text{SO}_3)_2(\text{NH}_3)_4]\cdot 4\text{H}_2\text{O}$ whereas with hydrochloric acid a remarkable orange ruthenamine $[\text{RuCl}(\text{NH}_3)_4\text{SO}_2]\text{Cl}$ containing neutral co-ordinated sulphur dioxide is formed. From this sulphito-chloride a number of similarly constituted salts, such as $[\text{RuBr}(\text{NH}_3)_4\text{SO}_2]\text{Br}$ and $[\text{Ru}(\text{NH}_3)_4\text{SO}_2\cdot\text{H}_2\text{O}](\text{NO}_3)_2$, can be obtained by double decomposition. With ammonia the sulphito-chloride yields the sulphite $[\text{RuSO}_3(\text{NH}_3)_5]\cdot 2\text{H}_2\text{O}$, which with mineral acid furnishes a pentammine series $[\text{Ru}(\text{NH}_3)_5\text{SO}_2]\text{X}_2$ containing sulphur dioxide. These bivalent ruthenamines are all diamagnetic. Oxidation of the chloride $[\text{RuCl}(\text{NH}_3)_4\text{SO}_2]\text{Cl}$ with iodine chloride, or of the corresponding bromide with bromine, leads to the tetrammines $[\text{RuCl}_2(\text{NH}_3)_4]\text{Cl}\cdot\text{H}_2\text{O}$ and $[\text{RuBr}_2(\text{NH}_3)_4]\text{Br}\cdot\text{H}_2\text{O}$, which have a *trans*-configuration since they differ markedly from the corresponding *cis*-derivatives. The constitution of the *cis*-tetrammines follows from their method of formation, which consists in treating the hydroxo-salt $[\text{RuOH}, 5\text{NH}_3]\text{S}_2\text{O}_6$ with oxalic acid, whereby the yellow oxalate $[\text{RuC}_2\text{O}_4, 4\text{NH}_3]\text{S}_2\text{O}_6$ is formed; hydrochloric acid then yields the *cis*-chloride $[\text{RuCl}_2(\text{NH}_3)_4]\text{Cl}, \frac{3}{4}\text{H}_2\text{O}$. The prolonged action of hydrogen chloride on this *cis*-tetrammine yields non-ionic $[\text{RuCl}_3(\text{NH}_3)_3]$ as a sparingly soluble, red deposit. The compounds of trivalent ruthenium are all paramagnetic with a moment of about 2 Bohr magnetons.

L. W. N. Godward and W. Wardlaw⁴ have obtained green crystalline salts of the types $\text{X}_2[\text{RuCl}_4]$ and $\text{X}_3[\text{RuCl}_5\cdot\text{H}_2\text{O}]$ containing bivalent ruthenium in a complex cation. These authors prepared pyridinium 2 : 2'-dipyridylum, and ethylenediammonium salts of the former type, and a trimethylammonium compound of the latter series by addition of these bases in hydrochloric acid to the deep blue solution resulting from electrolytic reduction of ruthenium trichloride in 6N-hydrochloric acid. These stable salts are diamagnetic.

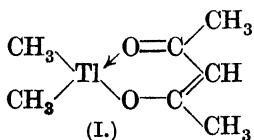
It has been found that the polypyridyls form a series of complex ruthenium derivatives containing the nitric oxide group.⁵ With $\text{K}_2[\text{RuNOCl}_5]$, 2 : 2'-dipyridyl behaves as a chelate group and yields the green internal complex $[\text{NORuCl}_3 \text{ dipy}]$ and the red salt $[\text{NORuCl}_2 \text{ 2dipy}][\text{NORuCl}_5]$. An extrusion of nuclear chlorine is effected by the tridentate base 2 : 2' : 2''-tripyridyl, resulting in the

⁴ *J.*, 1938, 1422.

⁵ (Sir) G. T. Morgan and F. H. Burstall, *J.*, 1938, 1675.

formation of brown, water-soluble $[\text{NORuCl}_2 \text{ tripy}]\text{Cl}, 3\frac{1}{2}\text{H}_2\text{O}$, and a further atom of chlorine is displaced to the anion when the quadridentate base 2 : 2' : 2'' : 2'''-tetrapyridyl is introduced into a molecule of nitrosoruthenium pentachloride, the salt $[\text{NORuCl tetpy}]\text{Cl}_2, 5\text{H}_2\text{O}$ being formed.

During the past few years considerable interest has been manifested in the structure of four-covalent metallic compounds. It was found that univalent compounds of copper, silver, and gold with a co-ordination number of four were tetrahedral in structure, whereas corresponding derivatives of bivalent copper and silver and trivalent gold possessed a planar configuration. A planar symmetry has also been shown to be present in certain four-covalent compounds of platinum, palladium, and nickel. An excellent summary of these facts has already been given.⁶ It has now been found⁷ by X-ray analysis that a planar arrangement is also apparent in the α -form of $[\text{CoCl}_2, 2\text{C}_5\text{H}_5\text{N}]$, which possesses a *trans*-configuration. This fact is of special interest, since a tetrahedral arrangement has already been found for the ion $[\text{CoCl}_4]^{--}$,⁸ thus showing that both types of spatial configuration can be manifested in unchelated derivatives of a bivalent metal. The structure of β - $[\text{CoCl}_2, 2\text{C}_5\text{H}_5\text{N}]$ is still uncertain, but it has been found that pink $[\text{MnCl}_2, 2\text{C}_5\text{H}_5\text{N}]$ is isomorphous with the α - $[\text{CoCl}_2, 2\text{C}_5\text{H}_5\text{N}]$ and must therefore possess a *trans*-planar configuration. A change in structure with a change in valency has also been discovered among derivatives of tin, lead,⁹ and thallium.¹⁰ In potassium stannous chloride, $\text{K}_2[\text{SnCl}_4], 2\text{H}_2\text{O}$, the four chlorine atoms are arranged in a plane with the tin atom, whereas in quadrivalent stannic iodide the distribution of halogen is tetrahedral. Similarly, with bivalent lead in $[\text{PbCl}_2, 2\text{CS}(\text{NH}_2)_2]$, the arrangement of addenda is planar in contrast to the tetrahedral configuration of such quadrivalent lead compounds as $\text{Pb}(\text{C}_6\text{H}_5)_4$. Among thallium derivatives, the complex salts $[\text{Tl } 4\text{CS}(\text{NH}_2)_2]\text{NO}_3$ (or Cl) containing the univalent element are planar, whereas in the trivalent thallic compound (I) a tetrahedral structure is regarded as most probable. In the foregoing survey of planar and tetrahedral types, it has been assumed that it is the central metallic atom which controls the arrangement of the co-ordinating units, but it is clear that other



⁶ *Ann. Reports*, 1936, **33**, 158.

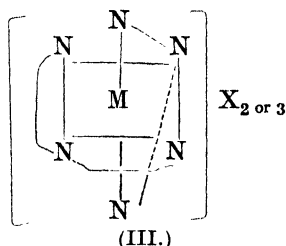
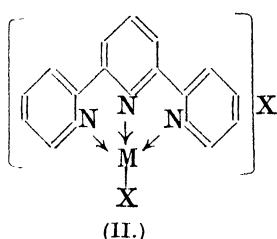
⁷ E. G. Cox, A. J. Shorter, W. Wardlaw, and W. J. R. Way, *J.*, 1937, 1556.

⁸ H. M. Powell and A. F. Wells, *J.*, 1935, 359.

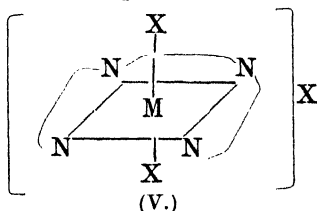
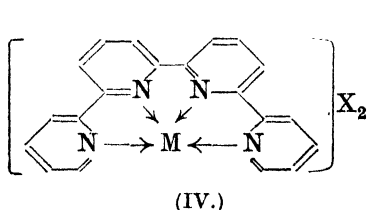
⁹ E. G. Cox, A. J. Shorter, and W. Wardlaw, *Nature*, 1937, **139**, 72.

¹⁰ *J.*, 1938, 1886.

considerations must be taken into account. The co-ordinating addenda may, owing to rigidity or size, be unable to take up an arrangement in keeping with the disposition of a metallic atom. This is particularly evident among the metallic derivatives of porphyrin and its allies (notably the phthalocyanines), where a relatively rigid macrocyclic ring imposes a planar structure on its metallic derivatives.¹¹ It is claimed that a similar imposition of a planar structure is apparent among the complex metallic salts containing 2 : 2' : 2''-tripyridyl (tripy) and 2 : 2' : 2'' : 2'''-tetrapyridyl (tetrapy), which are unable to encircle a tetrahedron without considerable distortion of the molecule.¹² The former, tridentate, base yields two series of well-defined salts: (a) those containing one molecule of base having formula (II) (where M is Cu^{II}, Ag^{II}, Zn, Cd, Hg, Pd, and Pt, and X is a univalent acid



radical), and (b) those with two molecules of the triamine exemplified by (III), where M is Fe^{II}, Co^{II} or ^{III}, Ni, Ru^{II}, Os^{II}, and Cr^{III}, and X is a univalent acid radical. Although (III) is octahedral, it is concluded that the two molecules of base are at right angles to one another and planar with respect to the central metallic atom. These salts are also notable for their unusual colour and exceptional stability. Complex salts with the quadridentate base

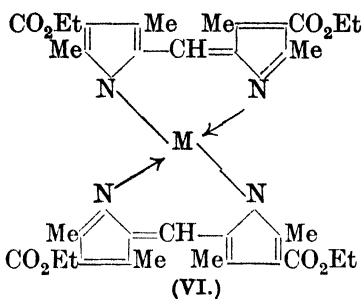


2 : 2' : 2'' : 2'''-tetrapyridyl contain only one molecule of base but yield types (IV) (where M is Fe^{II}, Co^{II}, Ni, Cu^{II}, Zn, Cd, and Pt^{II}, and X is a univalent acid radical) and (V) (where M is Co^{III} and Ir^{III}). These derivatives differ considerably in colour and stability from the foregoing salts with 2 : 2' : 2''-tripyridyl.

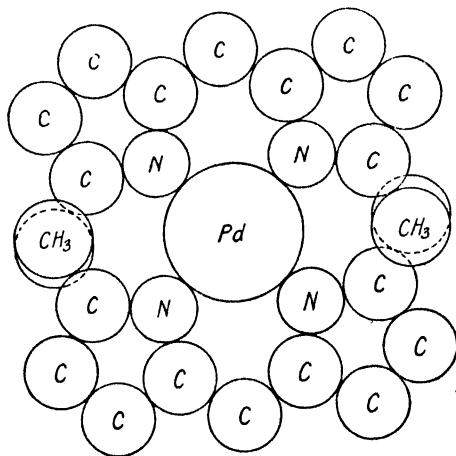
¹¹ *Ann. Reports*, 1937, **34**, 369.

¹² (Sir) G. T. Morgan and F. H. Burstall, *J.*, 1937, 1649; 1938, 1672.

The converse of the method whereby a metal ion is constrained to take up a planar configuration has also been attempted.¹³ A chelate group is chosen such that metallic derivatives of the type R_2M cannot be planar. These conditions prevail in metallic compounds of ethyl tetramethylpyrromethene-4:4'-dicarboxylate of type (VI), which must be non-planar owing to the mutual interference of four methyl groups which operate in a similar manner to that of 2:2'-disubstituted diphenyl derivatives. The effect is shown diagrammatically for the palladium compound in (VII).



(M = Co, Ni, Cu, Zn, Cd, and Pd.)



(VII.)

An interesting addition to the chemistry of ethylenediamine-cupric salts has been made by F. W. Chattaway and H. D. K. Drew,¹⁴ who have shown that the complex salt $[CuCl_2, en]$ is really the dimeric cuprichloride $[Cu_2en]CuCl_4$.

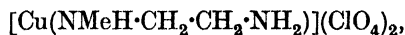
It follows that the corresponding sulphate $[CuSO_4, en] \cdot 3H_2O$ may be regarded as a dimeric cuprisulphate $[Cu_2en][Cu(SO_4)_2 \cdot 6H_2O]$, whereas hydrated cupric sulphate (blue vitriol), $CuSO_4 \cdot 5H_2O$, may be formulated as $[Cu, 4H_2O][Cu(SO_4)_2 \cdot 6H_2O]$. As bearing on the latter structure, it is significant that X-ray analysis of copper sulphate¹⁵ shows only four molecules of water surrounding the

¹³ C. R. Porter, *J.*, 1938, 368.

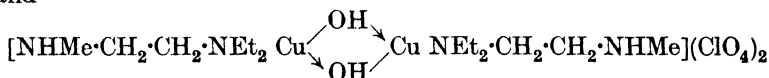
¹⁴ *J.*, 1937, 947.

¹⁵ C. A. Beevers and H. Lipson, *Proc. Roy. Soc.*, 1934, A, 146, 570.

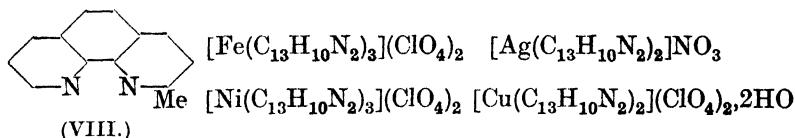
copper atom, the fifth being associated with two other water molecules and two oxygen atoms of a sulphate group. The tendency of ethylenediamine to form stable complex cupric salts is well known, but it has now been found that this effect is greatly reduced in *N*-alkylated ethylenediamines.¹⁶ Nevertheless, the perchlorates



and

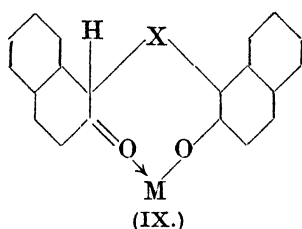


were obtained from alcoholic solution, but definite salts could not be isolated with $\text{NHPh}\cdot\text{CH}_2\cdot\text{CH}_2\cdot\text{NEt}_2$. Attention may be directed to the complex salts¹⁷ containing 3-methyl-4 : 5-phenanthroline (VIII) :



in which, it is claimed, the methyl group exerts no marked effect on the co-ordinating power of the two nitrogen atoms of the organic base.

Co-ordination compounds of the alkali metals of well-defined



(M = Li, Na, K, Rb.)

type¹⁸ are less plentiful than those of the transition elements, but further additions¹⁹ have been made recently by the production of alkali-metal salts of di-2-hydroxy-1-naphthyl sulphide (IX; X = S), di-2-hydroxy-1-naphthyl-methane (IX; X = CH₂), and di-2-hydroxy-1-naphthyl selenide (IX; X = Se). These compounds, which are normally hydrated (2 or 4H₂O), are

typical covalent derivatives, being soluble in organic solvents. The presence of a stable eight-membered ring is particularly noteworthy.

Recently, H. D. K. Drew and N. H. Pratt,²⁰ investigating the

¹⁶ P. Pfeiffer and H. Glaser, *J. pr. Chem.*, 1938, [ii], 151, 134.

¹⁷ P. Pfeiffer and W. Cristeleit, *ibid.*, p. 127.

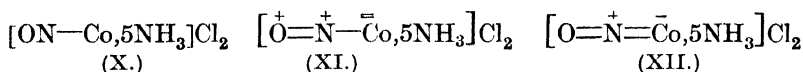
¹⁸ See *Ann. Reports*, 1933, 30, 98.

¹⁹ W. J. Evans and S. Smiles, *J.*, 1937, 727; V. Dvorkovitz and S. Smiles, *J.*, 1938, 2022.

²⁰ *J.*, 1937, 506.

interaction of molecular proportions of cobaltous chloride and ethylenediamine in a limited supply of air, found that the pink, insoluble cobaltochloride $[\text{CoOH}(\text{en})_2\text{H}_2\text{O}]\text{CoCl}_4$ was formed, and that addition of hydrochloric acid to the filtrate furnished green $[\text{CoCl}_2(\text{en})_2]\text{CoCl}_4\cdot\text{H}_2\text{O}$, both products being *trans*-derivatives. With more concentrated hydrochloric acid the former cobaltochloride decomposed with rupture of one ethylenediamine ring and formation of $[\text{CoCl}_3\text{enNH}_2\cdot\text{CH}_2\cdot\text{CH}_2\cdot\text{NH}_3]\text{Cl}$, a dihydrate of which was earlier recorded by S. M. Jørgensen.²¹

The way in which physical measurements assist in the determination of the structure of co-ordination compounds is well shown in a reinvestigation of the red and black forms of nitrosopentamminocobalt salts by (Mrs.) J. L. Milward, W. Wardlaw, and W. J. R. Way.²² The red chloride $[\text{NOCo},5\text{NH}_3]\text{Cl}_2$ obtained from the nitrate $[\text{NOCo},5\text{NH}_3](\text{NO}_3)_2\cdot 0\cdot5\text{H}_2\text{O}$ by cold concentrated hydrochloric acid is diamagnetic and yields the purpureo-chloride $[\text{CoCl},5\text{NH}_3]\text{Cl}_2$ on decomposition with hydrochloric acid. It is, therefore, regarded as a genuine tervalent cobaltic salt (X) in which nitric oxide is attached to cobalt in the same way as it is to carbon in organic nitrosyls. The corresponding black chloride, however,



is paramagnetic and yields a solution containing bivalent cobalt after decomposition with hydrochloric acid. In view of these results, the foregoing authors concluded that the black chloride is a hybrid of the two structures (XI) and (XII) in which the cobalt atom will act as if it were substantially bivalent. These electronic structures may also be applied to the complex nitrosoruthenium salts already described (p. 161).

Some interesting work has recently been carried out^{23,24} on the complex cyanides of rhenium, the only known members of which are salts of the hypothetical acid $\text{H}_3[\text{ReO}_2(\text{CN})_4]$. The British authors²⁴ prepare these salts either by reduction of alkali per-rhenate with hydrazine hydrate in presence of alkali cyanide, or better, by boiling hydrated rhenium dioxide with aqueous alkali cyanide and oxidising the product with hydrogen peroxide. These oxycyanides are normally yellow, brown, or red, but acid salts with 2 : 2'-dipyridyl, $(\text{C}_{10}\text{H}_8\text{N}_2\text{H})_2\text{H}[\text{ReO}_2(\text{CN})_4]\cdot 4\text{H}_2\text{O}$, and phenanthridine, $(\text{C}_{13}\text{H}_9\text{NH})_2\text{H}[\text{ReO}_2(\text{CN})_4]$, are pale blue. Rhenium is quinquevalent in these cyanides.

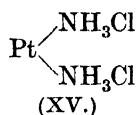
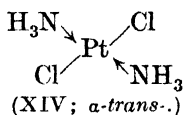
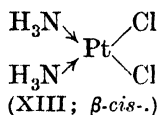
²¹ *J. pr. Chem.*, 1889, **30**, 24.

²² *J.*, 1938, 233.

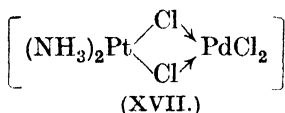
²³ W. Klemm and G. Frischmuth, *Z. anorg. Chem.*, 1937, **230**, 215.

²⁴ (Sir) G. T. Morgan and G. R. Davies, *J.*, 1938, 1858.

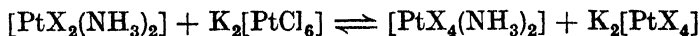
Platinum salts combine with an enormous range of inorganic and organic groups or molecules and many of these complex salts have been known for over 100 years. Yet the constitution of the isomeric diammines of type $[\text{PtCl}_2, 2\text{NH}_3]$ is still the subject of controversy. It is believed, on the one hand, that there are only two isomers which have a *cis*-(XIII) and a *trans*-(XIV) planar arrangement originally proposed by Alfred Werner, and on the other hand, that



there are three isomers: (a) the α -*trans*-diammine (XIV), (b) a β -diammine which is regarded as a substituted ammonium salt (XV), and (c) a γ -isomeride $[\text{H}_3\text{NClPtNH}_3\text{Cl}]$ (XVI) which is intermediate between (a) and (b), these structures being proposed by H. D. K. Drew, F. W. Pinkard, W. Wardlaw, and E. G. Cox.²⁵ Recently F. W. Chattaway and H. D. K. Drew²⁶ have brought forward further evidence in favour of the structure (XV) for the β -dichloride. Interactions of β - $[\text{PtCl}_2, 2\text{NH}_3]$ and palladous chloride in hydrochloric acid, or potassium palladochloride, furnish the two compounds $[\text{Pt}(\text{NH}_3)_2\text{Cl}]_2\text{PdCl}_6$ and $[\text{Pd}(\text{NH}_3)_2]\text{PdCl}_4$ in black and greyish-black crystals respectively. The former salt arises from aerial oxidation, and both salts are readily dissociated on warming with water. The authors conclude that these experiments show that the β -dichloride can and does act in the ionic forms $[\text{Pt}(\text{NH}_3)_2\text{Cl}]\text{Cl}$ and $[\text{Pt}(\text{NH}_3)_2]\text{Cl}_2$, but an alternative formulation (XVII) cannot be entirely excluded. It



is significant that β -diammines containing addenda other than ammonia have not so far yielded similar compounds, a fact which lends some support to the view²⁷ that the β -salts $[\text{PtCl}_2\text{X}_2]$ are of two types: (1) a large class of conventional *cis*-structure (XIII), and (2) a small class, including the ammonia compounds, in which chlorine atoms are united with nitrogen (XV). It was also observed that neither α - nor γ - $[\text{PtCl}_2(\text{NH}_3)_2]$ reacted with palladous chloride, but A. A. Grunberg and F. M. Filinov,²⁸ operating with potassium platinichloride, find that the equilibrium



(X = Cl, Br, CNS, or I) is established with both *cis*- and *trans*-

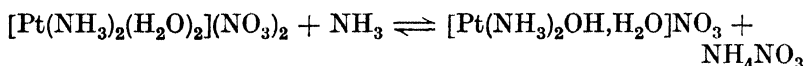
²⁵ *J.*, 1932, 993.

²⁶ *J.*, 1938, 198.

²⁷ H. D. K. Drew and H. Tress, *J.*, 1933, 38; 1935, 1212.

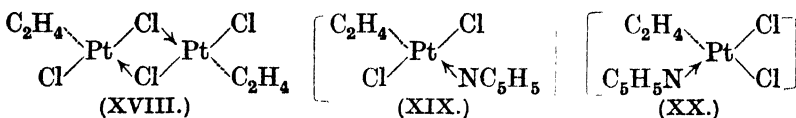
²⁸ *Bull. Acad. Sci. U.R.S.S., Ser. Chim.*, 1937, 1245.

compounds. New light on the behaviour of diamminoplatinous salts in aqueous solution has resulted from a study of their electrical conductivities: H. J. S. King²⁹ finds that there are two classes of diammine: (1) those which are practically non-electrolytes, such as the dichlorides and dihydroxides, and (2) those which are conductors, such as the *cis*- and *trans*-dinitrates, -dipicrates, and -sulphates. In the latter group the conductivity is such as to indicate the formation in solution of diaquo-salts of the type exemplified by $[\text{Pt}(\text{NH}_3)_2(\text{H}_2\text{O})_2](\text{NO}_3)_2$ which, however, could not be separated in the hydrated condition. Addition of ammonia to a solution of the dinitrate sets up an equilibrium which conductivity measurements indicate is in accordance with the scheme



The aquohydroxo-nitrate could not be isolated, but the hydroxo-nitrates (*cis* and *trans*) $[\text{Pt}(\text{NH}_3)_2(\text{OH})\text{NO}_3]$ were obtained in the solid state, and became hydrated on dissolving in water, with formation of univalent cations.

Among co-ordination compounds of platinum, those containing olefins are of considerable interest owing to the difficulty of providing an adequate electronic interpretation of their structure.³⁰ From the mixture resulting from heating sodium chloroplatinate and alcohol, yellow dimeric $(\text{PtCl}_2\text{C}_2\text{H}_4)_2$ (XVIII) and the salt $\text{K}[\text{PtCl}_3\text{C}_2\text{H}_4]$ can be isolated by suitable means.³¹ This process represents the classical preparation of Zeise, but a more convenient method³² of obtaining the former covalent derivative consists in bubbling ethylene through a suspension of platonic chloride in benzene at 70°.



Corresponding styrene, amylene, and *cyclohexene* derivatives can also be prepared, either by interactions of the olefin with platonic chloride in glacial acetic acid suspension or by heating the ethylene-platinous chloride with the less volatile hydrocarbon. The olefin is eliminated from these compounds by heat alone, the action of hydrochloric acid, or excess pyridine. The stereochemistry of the Zeise series of salts $\text{R}[\text{C}_2\text{H}_4\text{PtCl}_3]$ is interesting. With aqueous pyridine the salt $[\text{C}_2\text{H}_4\text{Pt}(\text{C}_5\text{H}_5\text{N})\text{Cl}_2]$ is formed and it is thought

²⁹ *J.*, 1938, 1338.

³⁰ *Ann. Reports*, 1936, 33, 177.

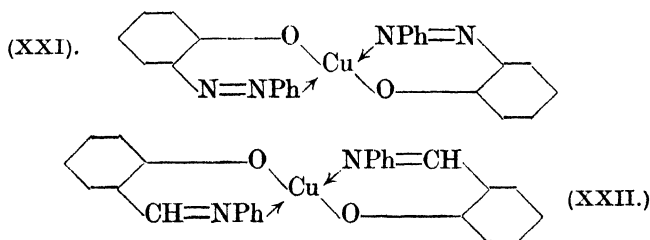
³¹ J. S. Anderson, *J.*, 1934, 971; 1936, 1042.

³² M. S. Kharasch and T. A. Ashford, *J. Amer. Chem. Soc.*, 1936, 58, 1733.

that this pyridine compound³³ has a *trans*-configuration (XIX), since excess pyridine yields *trans*-[PtCl₂(C₅H₅N)₂]. The action of ethylene on K[(C₅H₅N)PtCl₃] (a Cossa-type salt) yields an isomeric product of *cis*-configuration (XX). With hydrochloric acid, both *cis*- and *trans*-derivatives furnish C₅H₅NH[C₂H₄PtCl₃]. Ammonia can replace pyridine in the foregoing reactions.³⁴

It has been found that palladium salts also combine with hydrocarbons. Olefins replace benzonitrile in the complex [PdCl₂·2C₆H₅·CN] with formation of compounds of type [RPdCl₂]₂, where R = ethylene, styrene, *cyclohexene*, and *isobutylene*, which are less stable than the platinous derivatives.³⁵ By means of a distribution technique, it has also been found that silver salts co-ordinate with certain hydrocarbons such as butadiene, *cyclohexene*, etc., although solid compounds were not obtained in every case.³⁶

That metallic lakes of mordant dyes are co-ordination complexes is probably accepted in principle by most chemists, for it provides the most satisfactory explanation for the formation of these interesting and important substances. In an important memoir, H. D. K. Drew and J. K. Landquist³⁷ have considerably clarified the position with regard to the copper lakes of *o*-substituted azo-dyes. The copper lake of 2-hydroxyazobenzene (XXI) is anhydrous and shows no tendency to take up further addenda of co-ordination,



and the formation of a six-membered chelate ring rather than a five-membered ring is inferred from the marked similarity between this copper complex and that of salicylideneaniline (XXII), which must on structural grounds possess two six-membered rings. Similar constitutions have been deduced for the copper complexes of other 2-hydroxyazo-dyes. The copper compounds of *o*-carboxy-azo-dyes show perceptible differences from the foregoing hydroxy-

³³ I. I. Tscherniaev and A. D. Gelmann, *Compt. rend. Acad. Sci. U.R.S.S.*, 1936, **4**, 181; *Ann. Sect. Platine*, 1937, **14**, 77.

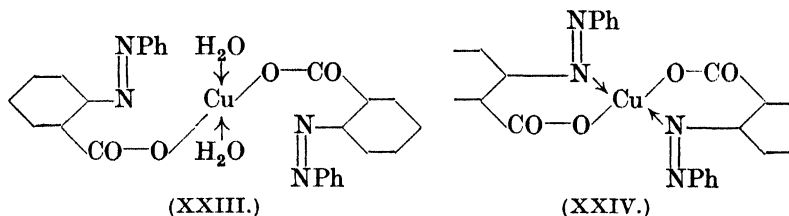
³⁴ A. D. Gelmann, *Sci. Rep. Leningrad State Univ.*, 1936, **2**, 5; *Compt. rend. Acad. Sci. U.R.S.S.*, 1937, **16**, 351.

³⁵ M. S. Kharasch, R. C. Seyler, and F. R. Mayo, *J. Amer. Chem. Soc.*, 1938, **60**, 882.

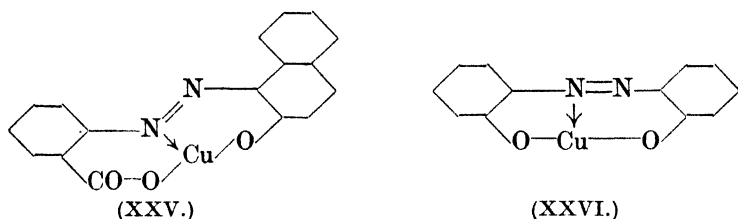
³⁶ S. Winstein and H. J. Lucas, *ibid.*, p. 836.

³⁷ *J.*, 1938, 292.

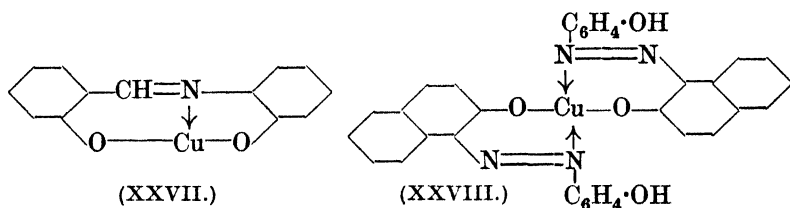
derivatives. Azobenzene-*o*-carboxylic acid yields the dihydrated salt (XXIII), which only furnishes the anhydrous salt (XXIV)



with some difficulty. With azo-dyes containing both an *o*-hydroxy- and an *o*-carboxy-group, such as *o*-carboxybenzeneazo- β -naphthol, there is production of a covalently unsaturated copper salt (XXV) which manifests its tendency to form four-covalent compounds by uniting with one molecule of aniline or pyridine. A similar degree of co-ordinative unsaturation prevails in the copper salt of 2 : 2'-dihydroxyazobenzene (XXVI) and other *oo'*-dihydroxyazo-dyes.



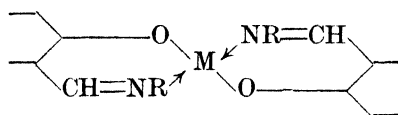
This unimolecular, intensely coloured, copper salt (XXVI) yields crystalline monopyridine and monoquinoline derivatives, thus increasing the co-ordination number of copper from three to four.



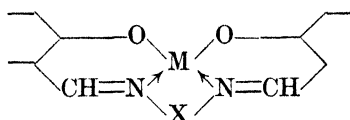
The similarity of (XXVI) to the copper derivative of salicylidene-*o*-aminophenol (XXVII) confirms the view that only one nitrogen atom is united to copper.

The removal of one *o*-hydroxy-group to the *m*- or the *p*-position leads to a copper lake of totally different type, as exemplified in (XXVIII). Two molecules of the dye then combine with one atom of copper, and the two *m*- or *p*-hydroxy-groups are uncombined. The constitution of copper lakes of azo-dyes containing sulphonic acid groups is more speculative, but the

primary reaction appears to be the formation of ionic cupric salts $(R\cdot SO_3)_2Cu$ which may be followed by conversion into an internal complex with suitable reagents (mild alkali), providing that there is a hydroxy-group in the *o*-position to the azo-group; a copper lake of type (XXVIII) is then formed in which the free hydroxy-groups are replaced by sulphonic acid groups. Numerous internal complex metallic compounds bearing a certain resemblance to the copper lakes just described have been prepared. The salicylidene derivatives^{38,39} can all be included in the general formulæ (XXIX) and (XXX) (where R is an aryl group, $-NH\cdot CO\cdot NH_2$, or H, X is $\cdot CH_2\cdot CH_2-$ or $o-C_6H_4<$,

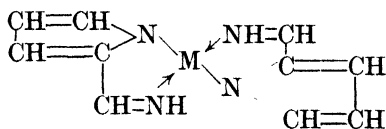


(XXIX.)

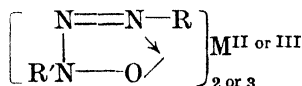


(XXX.)

and M is a bivalent metal, Cu, Zn, Ni). Attempts to resolve compounds of the type (XXX) were unsuccessful. Very similar to the foregoing are the metallic aldimines,³⁸ which are the same as (XXIX) and (XXX) with the oxygen atoms replaced by imino-groups. Certain pyrrole derivatives yield metallic complexes³⁸ of the type (XXXI), as well as those containing a bridge group



(XXXI.)



(XXXII.)

(compare XXX) which unites two pyrrole units. Hydroxytriazens also act as powerful chelate groups, forming highly-coloured metallic salts (XXXII) which, from their solubility in organic media and low melting points, are typical covalent derivatives.⁴⁰ Semicarbazide and substituted semicarbazides also act as chelate groups with metal ions, yielding complex derivatives (XXXIII) containing one, two, or three organic molecules to one atom of metal.^{41,42} Aminoguanidine acts in a very similar manner, yielding derivatives of the type (XXXIV).

³⁸ P. Pfeiffer, T. Hesse, H. Pfützner, W. Scholl and H. Thielert, *J. pr. Chem.*, 1937, [ii], 149, 217; P. Pfeiffer, W. Christeleit, T. Hesse, H. Pfützner and H. Thielert, *ibid.*, 1938, [ii], 150, 261.

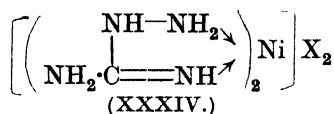
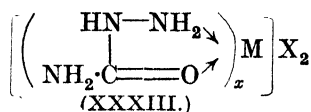
³⁹ L. Hunter and J. A. Marriott, *J.*, 1937, 2000.

⁴⁰ (Miss) M. Elkins and L. Hunter, *J.*, 1938, 1346.

⁴¹ K. A. Jensen and E. Ranke-Madsen, *Z. anorg. Chem.*, 1936, 227, 25.

⁴² G. S. Smith, *J.*, 1937, 1354.

In the foregoing survey, the co-ordination compounds have all been metallic complexes, and it is fitting therefore to conclude with reference to co-ordination between non-metals or metalloids.



Good examples of these substances are the sulphilimines⁴³ $\text{R}_2\text{S} \rightarrow \text{N} \cdot \text{SO}_2 \cdot \text{C}_7\text{H}_7$, phosphinimines $\text{R}_3\text{P} \rightarrow \text{N} \cdot \text{SO}_2 \cdot \text{C}_7\text{H}_7$, and arsini-
mines $\text{R}_3\text{As} \rightarrow \text{N} \cdot \text{SO}_2 \cdot \text{C}_7\text{H}_7$, which arise from the interaction of organic sulphides, phosphines, and arsines respectively with chlor-
amine-T, $\text{CH}_3 \cdot \text{C}_6\text{H}_4 \cdot \text{SO}_2 \cdot \text{NNaCl} \cdot 3\text{H}_2\text{O}$. These derivatives are struc-
turally analogous to the corresponding oxides $\text{R}_2\text{S} \rightarrow \text{O}$, $\text{R}_3\text{P} \rightarrow \text{O}$,
and $\text{R}_3\text{As} \rightarrow \text{O}$.

F. H. B.

F. H. BURSTALL.

F. G. MANN.

H. TERREY.

O. J. WALKER.

R. WHYTLAW-GRAY.

⁴³ F. G. Mann, *J.*, 1932, 958; F. G. Mann and E. J. Chaplin, *J.*, 1937, 527.

CRYSTALLOGRAPHY.

1. INTRODUCTION.

IN the early days of X-ray crystallography there was naturally a tendency to select for examination substances which occurred in large, well-formed crystals and presented no technical difficulties, and for this reason many structures were prematurely and imperfectly analysed. The numerous references¹ in current literature to improved methods for studying substances in all stages of aggregation and at almost any temperature or pressure serve to emphasise the fact that there is now no reason for selecting one substance rather than another for analysis other than its relatively greater importance. An absolute standard of importance in crystallography is a somewhat barren conception, and we find that the determinative factor is usually the significance of a substance for one or more of the many sciences which require structural information for their full development; the mere enumeration of these sciences sufficiently emphasises the key position occupied by crystallography. In the present Report special sections are devoted to topics which have obvious connections with metallurgy, soil science and ceramics, and biochemistry, and the general sections on inorganic and organic structures record advances which, in many cases, have been inspired by theoretical chemistry, and in others provide accurate data for a more detailed examination of the problems of chemical binding. In many fields, however, the contributions of crystallography are not yet as extensive as they should be; for example, the Faraday Society's stimulating discussion² on reactions in solids emphasised the great need of structure analysis specifically organised for the development of this subject.

An encouraging feature of current researches is the increasing tendency to use other physical methods in conjunction with X-rays, and on this account alone the appearance of the first book in English on the fundamentals of crystal physics³ is particularly

¹ R. B. Jacobs, *Physical Rev.*, 1937, **51**, 999; **54**, 325; O. P. Hendershot, *Rev. Sci. Instr.*, 1937, **8**, 436; C. Gamertsfelder and N. S. Gingrich, *ibid.*, 1938, **9**, 154; F. Schossberger, *Z. Krist.*, 1937, **98**, 259; 1938, **99**, 341; W. Hume-Rothery and P. W. Reynolds, *Proc. Roy. Soc.*, 1938, *A*, **167**, 25; A. Goetz, R. B. Jacobs, and O. B. Jackson, *Physikal. Z.*, 1937, **38**, 998.

² *Trans. Faraday Soc.*, 1938, **34**, 822.

³ W. A. Wooster, "A Text-book on Crystal Physics," Cambridge Univ. Press, 1938.

timely. The value of optical and magnetic methods has been established for some time, and the introduction of infra-red and dielectric measurements on single crystals ⁴ foreshadows the development of techniques which will not only yield results of great interest in themselves but will considerably assist structure analysis, particularly of organic compounds. The correlation of structural information from X-ray analysis with the energy values and other data derived from thermal, infra-red, and dielectric measurements for appropriate key substances should afford a means of shortening considerably the analysis of many compounds and of predicting the properties of others unsuited to exact analysis. In this connection a survey ⁵ of crystal structures in relation to thermal conductivity is of interest.

Physical properties are particularly valuable also in the study of those substances which do not conform to the strict geometrical laws of crystallography and consequently are not always susceptible of exact analysis by X-rays. These substances, which are now so numerous as to call for detailed classification ⁶ and figured largely in a recent discussion ⁷ of the German Bunsen Society, fall into four main types according as the kind of irregularity is :

- (1) Occupation of equivalent lattice points by different molecules, atoms, or ions.
- (2) Non-occupation of some lattice points.
- (3) Occupation of inter-lattice points by molecules, atoms, or ions.
- (4) Rotation or variable orientation of molecules or groups.

Some aspects of (2) and (3) were discussed in these Reports last year; alloys afford frequent examples of (1), and (4) is of common occurrence among organic compounds. These irregularities, which have so far been studied chiefly by thermodynamic and electrical methods, are of great theoretical interest and are intimately connected with, *inter alia*, problems of plasticity, diffusion, and the structure of liquids.

E. G. C.

2. TECHNIQUE.

There have appeared during the past year various publications which in the Reporter's opinion ignore certain fundamental limitations of structure analysis and give an erroneous impression of

⁴ *E.g.*, R. C. Evans, *Phil. Mag.*, 1937, **24**, 70; G. Busch, *Helv. Physica Acta*, 1938, **11**, 269; J. W. Ellis and J. Bath, *J. Chem. Physics*, 1938, **6**, 221.

⁵ H. D. Megaw, *Z. Krist.*, 1938, **100**, 58.

⁶ W. Nowacki, *ibid.*, p. 77.

⁷ F. C. Frank, *Nature*, 1938, **142**, 1166.

its present power, and it may therefore be opportune to survey briefly the existing position of the technique of the subject.

As is well known,⁸ the objects of experimental technique are, first, to determine the cell dimensions and space group of the substance under investigation, and secondly, to determine for as many planes (h, k, l) as possible the integrated reflection intensities and thence the squares of the structure amplitudes F^2_{hkl} . The object of interpretative technique is to find an atomic arrangement consistent with all the experimental data, i.e., with the F^2 's; this object may be attained by "trial and error" or by direct synthesis leading to one-, two-, or three-dimensional electron distributions.

Improved methods for determining cell dimensions, analysing photographs, measuring intensities, etc. (including the increasing use of strictly monochromatic radiation), continue to be devised, and it is fair to say that in general there is no serious obstacle to the determination of a series of F^2 's adequate both in number and in accuracy for the purposes of an ordinary structure analysis. Interpretative technique is, however, not yet free from a major difficulty arising from the fact that the quantity F required for direct Fourier synthesis is in general complex and therefore has a phase angle which cannot be deduced from the experimental value of F^2 . In many cases an approximate structure can be found by trial and error, and the phase angles so determined utilised in an F -synthesis which if necessary must be successively refined, but the laborious nature of trial and error calculations has led to the introduction of the so-called direct (Patterson) methods of synthesis in which the experimentally observed F^2 's are used, so that the resulting contour diagrams give, not atomic positions, but inter-atomic vectors. In not too complicated cases the information obtained in this way enables the F -synthesis to be effected. An elegant algebraic method of analysis has been proposed by M. Avrami,⁹ which, in the absence of data on phase angles, yields the same information as the Patterson method, over which it is claimed to have some advantage on account of the slow convergence of the F^2 -series. The algebraic method, however, is clearly less general in its scope, since it fails in just those cases which are most difficult of solution by other methods, viz., those in which the highest available values of h, k , or l are less than the number of parameters in the structure; it is significant that essentially the same method

⁸ Recent accounts of the methods of crystal analysis are given in "Angewandte Kristallstrukturlehre," E. Brandenberger, Berlin, 1938, and in "Röntgenanalyse von Kristallen," J. M. Bijvoet and N. H. Kolkmeijer, Amsterdam, 1938.

⁹ *Physical Rev.*, 1938, [ii], 54, 300.

(in a less general form) has had no application, so far as the Reporter is aware, since its publication ¹⁰ over five years ago.

It is clear that, corresponding to a given F^2 series (which summarises the experimental data), there is an infinity of F -series, only one of which represents the actual crystal structure; most of these can be eliminated by applying the criterion that the electron density in a real crystal must everywhere be positive (or zero), but since it is always possible to find an F sufficiently small to enable its phase angle to be varied without producing any negative electron densities, it is not possible in general to determine a unique F -series corresponding to an F^2 -series. The final test of the correctness of a proposed structure must be the agreement between observed F^2 's and the values calculated from the atomic positions and scattering factors. In this connection the determination of accurate atomic scattering factors is of considerable importance.¹¹

In discussing many aspects of structural crystallography (*e.g.*, space-group theory) it is convenient to regard the actual atomic arrangement as being replaced by a point distribution; this procedure, however, is liable to be misleading when used in the discussion of the interpretation of vector maps ¹² (F^2 -syntheses) if for no other reason than that the important conception of resolving power is inapplicable to point distributions. It is generally accepted that the resolving power in a Fourier synthesis of the type used in structure analysis is determined by the ordinary diffraction theory; ¹³ this indicates that it is impossible to distinguish two peaks in a contour map if their distance apart is less than $0.61d_0$, where d_0 is the lower limit to the spacing of the planes whose F 's (or F^2 's) are utilised to synthesise the contour map. Consideration of resolving power reveals a significant difference between F -series and F^2 -series. The former represents the electronic distribution in a crystal, and consequently peaks (representing atoms) cannot occur closer than an atomic diameter, *i.e.*, 1 Å. or more; since d_0 can be made less than 1 Å. (for truly crystalline substances), it follows that individual atoms can always be resolved by means of a suitable F -series, however complex the structure, the only difficulty being, as pointed out above, the determination of the phases of the F 's. On the other hand, since an F^2 -series exhibits maxima corresponding to the separation of *pairs* of maxima in the corresponding F -series, their number increases rapidly with the volume of the unit cell, and their average distance apart becomes less than the resolving

¹⁰ K. Banerjee, *Proc. Roy. Soc.*, 1933, *A*, **141**, 188.

¹¹ *E.g.*, G. W. Brindley and P. Ridley, *Proc. Physical Soc.*, 1938, **50**, 96.

¹² I. Langmuir and D. M. Wrinch, *Nature*, 1938, **142**, 581; D. M. Wrinch, *ibid.*, p. 955; E. H. Neville, *ibid.*, p. 994.

¹³ W. L. Bragg and J. West, *Phil. Mag.*, 1930, **10**, 823.

power. In organic compounds there are roughly 60 atoms per 1000 Å.³, so that the three-dimensional F^2 -synthesis for such a substance exhibits roughly $3600n^2$ maxima, where 10^3n Å.³ is the volume of the unit cell; in practice, this may be reduced to (say) $900n^2$ on account of symmetry, but even so, the average separation of maxima becomes less than the resolving power (say 0.5 Å.) when n exceeds 4, and the probability of two maxima being unresolvable is evidently very high for much smaller unit cells. If the structure contains a small number of heavy atoms, the maxima due to these will stand out on the almost uniform background due to the lighter atoms. Experience shows that the value of the Patterson method lies in this; it can be relied upon to fix the positions of heavy atoms, and in some cases to identify peaks corresponding to distances between heavy and light atoms, but except in the simplest cases (*e.g.*, pentaerythritol) it cannot determine the positions of light atoms (*e.g.*, carbon, nitrogen and oxygen). (It should be noted that the preceding discussion applies to three-dimensional summations and that conditions are less favourable in the case of two-dimensional series on account of the much greater probability of maxima overlapping.) Apart from the effects of heavy atoms, the peaks observed in the Patterson diagrams of complicated organic molecules are due to the superposition of many interatomic vectors, and can be used to determine only the general outlines of the structure; *e.g.*, in the case of insulin¹⁴ the lower limit of spacing for which reflections were observed was 7 Å., so that the resolving power of the F^2 -series is of the order of 4 Å., and therefore, although the synthesis may be used to test an assumed structure, it is clearly impossible at present to deduce a unique atomic arrangement in detail from it.

A further suggestion¹² in connection with the F^2 -series is that, if the structure of a substance can be represented by a continuous electron distribution (F -series), then the associated F^2 -series should show maxima corresponding, not only to distances between maxima (atoms) in the electron distribution, but also to distances between minima (regions, between atoms, of low electron density).¹⁵ It is readily seen, however, that maxima in the F^2 -series due to this second cause are negligible. In two-dimensional syntheses of typical organic compounds the mean electron density is about $2e/\text{Å.}^2$ while the maxima (*e.g.*, at the centres of carbon atoms) exceed $7e/\text{Å.}^2$. Since the minimum possible electron density is zero, the heights of peaks in the F^2 -series due respectively to atom-atom and minimum-minimum distances will be roughly in the ratio $(7-2)^2$ to $(2-0)^2$, *i.e.*, 6 to 1, so that no error will be introduced by

¹⁴ See p. 201.

¹⁵ I. Langmuir and D. M. Wrinch, *loc. cit.*, ref. (12).

assuming that all observed peaks are associated with interatomic vectors.

The preceding discussion has emphasised limitations of synthetic methods which are recognised by crystallographers, and it is of interest to note that in a number of widely different structure analyses carried out in the past year an almost identical procedure has been adopted, *viz.*, use of F^2 -synthesis to locate heavy atoms, calculation of phase angles of the more important F 's followed by F -synthesis, and finally, refinement of atomic co-ordinates by trial and error methods. A development of interpretative technique which may be expected in the near future is the simplification and improvement of structure amplitude calculations and their extended application by the method of Fourier transformations. This method,¹⁶ which provides a means of systematising trial and error calculations, is likely to be of particular value in the case of those substances where the approximate shape of the molecule can be assumed from chemical evidence but where little or no assistance can be derived from optical or magnetic data; the chief obstacle to its employment at present is undoubtedly the laborious nature of the calculations.

Although the analysis of complex structures is still a matter of some difficulty, the available methods are more than adequate for the complete determination of simple structures, and the question arises as to whether it is possible to push the analysis in such cases beyond the mere determination of atomic positions and to obtain electron-density distributions of sufficient accuracy to discriminate between the various types of chemical binding. It is evident that in analyses of the required precision, various considerations would loom large which are of small importance in ordinary crystal analyses. It would be necessary to use strictly monochromatic radiation, and to ascertain whether under the conditions of the experiment the incident X-ray beam contained a plane-polarised component. The actual measurement of intensities would require considerably higher accuracy than is usually attained, and the corrections for extinction and "indirect excitation"¹⁷ would require to be much more carefully estimated. Although experimental details are not yet available, R. Brill and his co-workers¹⁸ claim to have attained the necessary precision in Fourier analyses of sodium chloride, diamond, hexamethylenetetramine, and magnesium, typical representatives of ionic, covalent, van der

¹⁶ See, *e.g.*, P. P. Ewald, *Z. Krist.*, 1935, **90**, 493.

¹⁷ M. Renninger, *Naturwiss.*, 1937, **25**, 43; *Z. Krist.*, 1937, **97**, 107.

¹⁸ H. G. Grimm, R. Brill, C. Hermann, and C. Peters, *Naturwiss.*, 1938, **26**, 29, 479; R. Brill, *Angew. Chem.*, 1938, **51**, 277.

Waals, and metallic structures respectively. For the first two substances their results are in accordance with expectation: the electron density falls to zero between chlorine and sodium ions but remains at a level of nearly $2e/A.^2$ between the carbon atoms in diamond, indicating the real existence of covalent bonds. Their conclusions with regard to hexamethylenetetramine and magnesium are, however, not likely to command general acceptance without considerably more evidence. The contour diagram of the former substance shows at certain points between molecules a density of nearly $1e/A.^2$, which is interpreted as indicating some form of hydrogen bond between the nitrogen and carbon atoms of adjacent molecules, and small protuberances in the contour lines around carbon atoms are said to represent hydrogen atoms. In the case of magnesium, the electron density between atoms differs from zero by an amount corresponding to the distribution of the conductivity electrons uniformly throughout the structure. It appears from a remark made by the authors that they are uncertain of the phase angle of F_{222} for diamond, and the same uncertainty probably occurs for other weak reflections; it should also be pointed out that the detection of an electron density due to conductivity electrons is contrary to all modern views, according to which conductivity electrons can give rise only to incoherent scattering of X-rays. P. Debye,¹⁹ in connection with the development of a method for determining the number of conductivity electrons from observations on incoherent scattering, has shown that the coherent scattering (contributing to lattice reflections utilised in structure analysis) is completely negligible.

E. G. C.

3. TERNARY ALLOY SYSTEMS.

The X-ray powder method is a powerful means for investigating complicated ternary alloy systems. It gives information which is not obtainable by use of the older methods, and enables phase-diagrams to be worked out from the beginning with reasonable speed and accuracy.

Until comparatively recently X-ray work was almost entirely confined to binary systems. Here its contribution mostly consisted in the fundamental task of solving the structures. Its application to problems of phase equilibria consisted for the most part in the more accurate delineation of the phase boundaries, the general outlines of all the most important binary systems having already been drawn by the classic methods of metallography.

Microscopic methods are less easy to apply to complicated ternary

¹⁹ *Physikal Z.*, 1937, **38**, 161; cf. W. Scharwächter, *ibid.*, p. 165.

systems, for the microscope cannot give the composition of a ternary phase where this is mixed with a second or third constituent. It is therefore very difficult to trace the course of the complicated reactions occurring in ternary alloy systems. X-Rays provide a necessary tool for this purpose, and whether used in conjunction with the microscope or separately, they are probably essential for the complete understanding of many ternary systems of technical importance. Above all, X-rays offer an infallible means for the identification of structures, whether solid solutions or compounds. An accurate measurement of the lattice spacings leads to a knowledge of the exact composition of a solid solution which is in equilibrium with a given compound, a point which is often of considerable importance.

Of course, many ternary equilibrium diagrams have already been partly worked out by the older methods, though these are more and more being supplemented by X-ray data. Very important work has recently been done by M. L. V. Gayler¹ on the dental amalgams, which are alloys of silver, tin, and mercury. As part of this research, the constitution of the ternary alloys was determined. It is suggested that seven invariant reactions take place, and on this basis a new theory is proposed to explain the changes occurring during the setting of dental amalgams. Another important investigation on a ternary system recently carried out by the usual thermal and microscopic methods, but supplemented by X-rays, is that of W. O. Alexander² on the copper-nickel-aluminium system.

Of primary importance is the study of the reactions taking place during solidification, which has in the past proceeded mainly from the interpretation of thermal curves. No doubt, high-temperature X-ray powder photographs will play an important part in future developments. Cameras such as that recently designed by W. Hume-Rothery and P. W. Reynolds³ will soon be an indispensable adjunct to studies of ternary systems. At present the use of high-temperature X-ray cameras is mainly confined to binary systems, as, *e.g.*, in the work of E. A. Owen and E. L. Yates⁴ on the coefficient of expansion of iron-nickel alloys.

It is, however, at lower temperatures that the use of X-rays is especially valuable. Here, thermal curves may give misleading results, for the alloys are often too sluggish to react during the time of cooling. Long periods of annealing, followed by X-ray powder

¹ *J. Inst. Metals*, 1937, **60**, 379, 407.

² *Ibid.*, 1938, **62**, advance copy.

³ *Proc. Roy. Soc.*, 1938, **A**, 167, 25.

⁴ *Proc. Physical Soc.*, 1937, **49**, 17, 178.

photographs, should reveal the true equilibrium conditions. It will then be possible to distinguish between the different types of reaction which may take place in ternary systems. As an alloy is cooled from the molten state to room temperature, any one of the following reactions may take place :

$A + B \rightleftharpoons C$ (eutectoid if solid, eutectic if C is liquid)

$A \rightleftharpoons B + C$ (peritectoid if solid, peritectic if C is liquid)

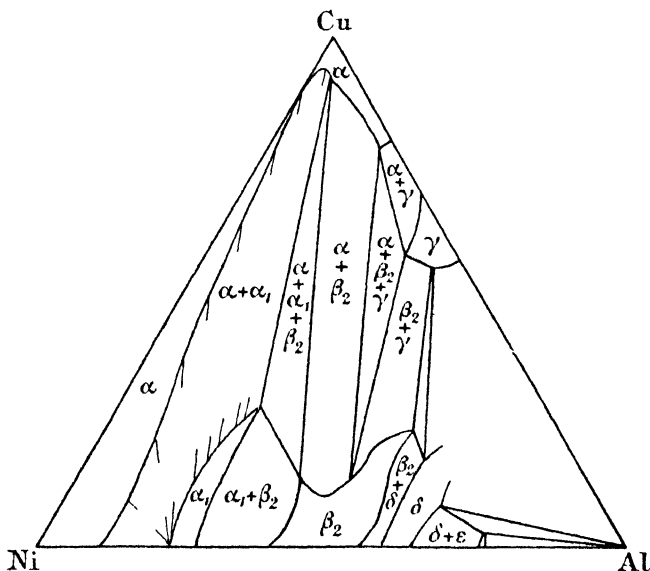
$A + B + C \rightleftharpoons D$ (monogenetic solution D)

$A + B \rightleftharpoons C + D$ (bigenetic solution D)

$A \rightleftharpoons B + C + D$ (trigenetic solution D)

(Read from left to right on heating, right to left on cooling.)

The reactants in the above equations may all have different structures, though this is not necessarily the case. For example,



both A and B may be face-centred cubic but with different compositions.

On the assumption that these reactions have been carried to completion down to a given temperature, it is possible to investigate the isothermal phase equilibrium diagram at that temperature. This consists of a mosaic of single-phase, two-phase, and three-phase areas, a typical example, with some of the more complicated regions omitted, being shown in the figure (A. J. Bradley and H. Lipson ⁵). The single-phase areas are in general bounded by curved

⁵ *Proc. Roy. Soc.*, 1938, A, 167, 421.

lines, and the three-phase areas are triangles, the corners of which give the compositions of the three phases. In a two-phase region the compositions of the phases, though no longer invariant, can be found for any given alloy from the directions of the tie-lines which are indicated by dashes (shown in the $\alpha_1 + \alpha$ region only). This is a specially valuable contribution of the X-ray method, though W. Köster and W. Dannohl⁶ have shown that magnetic measurements may sometimes be used for the same purpose.

The first important investigation of a ternary alloy system by purely X-ray methods was that of E. Persson⁷ on the copper-manganese-aluminium system. Later, F. R. Morral⁸ examined the iron-rich iron-aluminium-carbon system. Following these pioneer investigations, A. G. H. Anderson and E. R. Jette⁹ made a more comprehensive survey of the iron-chromium-silicon system, which was important on account of the use of a new method for fixing phase boundaries in ternary systems. Finally, A. J. Bradley and A. Taylor¹⁰ and A. J. Bradley and H. Lipson⁵ have worked out complete constitutional diagrams for given heat-treatments in the case of the iron-nickel-aluminium and copper-nickel-aluminium systems. In preparing such preliminary phase-diagrams the essential point is to fix the positions of the corners of the three-phase fields, which is readily done from a comparison of a small number of photographs.

A. G. H. Andersen and E. R. Jette¹¹ have devised a method for applying lattice-spacing measurements to the determination of phase boundaries in ternary systems, the principle of which is that the lattice spacing contours show abrupt changes in direction on crossing from a two-phase field to a single-phase area. In practice, difficulties may sometimes arise where the changes in direction are only slight, especially when the lattice spacing contours in the single-phase fields show serious departures from Vegard's law. The phase boundaries can then be fixed solely from a visual estimate of the proportions of the phases present in two-phase alloys. Though not leading to highly accurate results, this method is sufficiently reliable for the construction of a first approximate phase diagram, as, *e.g.*, in the case of the above iron- and copper-nickel-aluminium systems.

In these diagrams it is surprising to find alloys consisting of two-phases which have, not merely the same type of structure, but also

⁶ *Z. Metallk.*, 1935, **27**, 220.

⁷ *Z. Physik*, 1929, **57**, 115.

⁸ *J. Iron Steel Inst.*, 1934, **130**, 419.

⁹ *Trans. Amer. Soc. Metals*, 1936, **24**, 375.

¹⁰ *Proc. Roy. Soc.*, 1938, **A**, **166**, 353.

¹¹ *Trans. Amer. Soc. Metals*, 1936, **24**, 519.

almost the same lattice spacings. For example, in the former system there is a range of alloys containing two body-centred cubic phases in equilibrium, whereas in the latter system two face-centred cubic structures are often present in the same alloy. At certain compositions, lattice spacings are absolutely identical, and the only differences are the presence of superlattices in one phase, but not in the other. Even this distinction may not always be found, so that the interpretation of isolated X-ray photographs is to be avoided at all costs. A complete range of compositions must be examined if trustworthy results are to be obtained.

Some interesting results have been obtained in structural investigations on ternary systems. It is often found that the ternary intermetallic compounds and solid solutions are analogous in structure to certain phases found in binary systems; *e.g.*, F. Laves and S. Werner¹² have found that the binary alloy Mg_2Zn is isomorphous with $\text{Mg}_3\text{Cu}_7\text{Al}_{10}$, both being cubic (O_h). This falls into line with the earlier observation that MgCuAl is isomorphous with MgZn_2 , while MgNiZn is isomorphous with MgCu_2 . Both these two types of structure are also found in each of the ternary systems Mg-Cu-Zn , Mg-Ag-Zn , Mg-Cu-Si , and Mg-Co-Zn .¹³ In accordance with the principle first laid down by Hume-Rothery, analogous structures are in each case found at about the same ratio of valency electrons to atoms.

The application of this rule to the phases found in ternary systems is difficult in the case of the transition elements. For example, P. Rahlfs¹⁴ has found four new phases of a body-centred cubic type with superlattices. These are: $(\text{Cu,Ni})_3\text{Sn}$, $a' = 5.946 \text{ \AA.}$; $(\text{Cu,Ni})_3\text{Sb}$, $a' = 5.857 \text{ \AA.}$; Ni_2MgSn , $a' = 6.097 \text{ \AA.}$; Ni_2MgSb , $a' = 6.050 \text{ \AA.}$ It thus appears that nickel may replace copper as though it, too, were univalent, whereas in general this element must be reckoned as null-valent when applying the Hume-Rothery rule. On the other hand, in the copper-nickel-aluminium system copper replaces nickel quite extensively in the phases Ni_3Al and Ni_2Al_3 , which extend up to the compositions Ni_2CuAl and NiCuAl_3 respectively. Such facts show the need for avoiding too literal an interpretation of the Hume-Rothery rule.

F. Laves¹⁵ has shown that it is possible to prepare a continuous series of ternary solid solutions extending between the composition AgCd_3 and pure magnesium. All these alloys have the same type of hexagonal close-packed structure, suggesting that the binding forces in metallic magnesium are not essentially different from those

¹² *Z. Krist.*, 1936, **95**, 114.

¹³ F. Laves and H. Witte, *Metallw.*, 1936, **15**, 15, 840.

¹⁴ *Ibid.*, 1937, **16**, 640.

¹⁵ *Naturwiss.*, 1936, **24**, 742.

in AgCd_3 , which is regarded as a typical Hume-Rothery compound. On the other hand, W. Hume-Rothery and G. V. Raynor¹⁶ have shown that the extension of ternary solid solutions depends on factors other than electron concentration. For example, Mg_2Sn does not dissolve any appreciable quantity of aluminium or indium even when the compositions are made up to give the correct proportions of electrons to atoms. The same workers¹⁷ have recently discussed the various other factors which must be taken into consideration in formulating a theory of alloys, the chief of which is the size-factor.

K. Riederer¹⁸ has examined the structures found in the system Al-Mg-Zn and finds a body-centred cubic structure for $\text{Al}_2\text{Mg}_3\text{Zn}_3$ with 160 atoms in the unit cell. He has also investigated the Al-Mg-Cd system,¹⁹ drawing up a ternary diagram for 230° . H. Witte²⁰ has examined some Mg-Zn-Ag alloys, also using X -ray methods.

It is beyond the scope of the present account to describe the many investigations of ternary alloy systems which are being carried out by other methods. Reference may be made to the investigations of W. Köster and his co-workers,²¹ on the systems Co-Mn-Al , Co-Mn-Cu , Fe-Co-V , Mn-Al-Tl , and Mn-Cd-Tl . Other recent results are those of J. L. Haughton²² on the system Ag-Al-Mg , and of D. Hanson and W. T. Pell-Walpole²³ on Sb-Cd-Sn . C. H. M. Jenkins, E. H. Bucknall, C. R. Austin, and G. A. Mellor²⁴ have investigated the Fe-Cr-Ni system.

A. J. B.

4. CRYSTAL CHEMISTRY.

With the progress of crystal chemistry the number of essentially new structure types discovered each year diminishes, particularly among simple substances, and it is interesting to observe that uranium, one of the last of the elements to be analysed,¹ appears to have a structure unlike that of any other, consisting of a hexagonal close-packed arrangement deformed in such a way that each atom is bonded to four neighbours only, two bonds being collinear and the other two at 127° to each other in a plane at right angles to the first pair.

The structures of various oxides, halides, sulphides, and other relatively simple compounds have been determined, but the majority

¹⁶ *Phil. Mag.*, 1938, [vii], **25**, 335.

¹⁷ *Ibid.*, **26**, 129.

¹⁸ *Ibid.*, 1938, **30**, 15.

²¹ *Z. Metallk.*, 1938, **30**, 281, 330.

²² *Ibid.*, 1937, **61**, advance copy.

¹ C. W. Jacob and B. E. Warren, *J. Amer. Chem. Soc.*, 1937, **59**, 2588.

¹⁸ *Z. Metallk.*, 1936, **28**, 312.

²⁰ *Z. angew. Min.*, 1937, **1**, 83.

²³ *J. Inst. Metals*, 1938, **62**, 175.

²⁴ *J. Iron Steel Inst.*, 1937, (2), 187.

of publications during the year have been devoted to more complex structures. Although, in general, the increase in complexity of substances studied has been accompanied by an increase in the extensiveness of the data employed for their analyses, this is not universally the case, and some proposed structures fall short of the accuracy desirable, on account of the small number of reflection intensities employed. In order that atoms shall be located with an accuracy of a few hundredths of 1 Å., it is necessary, except in the simplest cases, to employ at least 100 intensities; visual estimates of many intensities are likely to give a better picture of the structure than the most accurate measurement of a few.

Structures containing linear groups include sodium cyanide,² sodium isocyanate,³ potassium hydrofluoride KHF_2 ,⁴ and ammonium chlorobromiodide.⁵ In the cubic modification of the cyanide (NaCl structure) the CN groups are rotating, and both in this and in the low-temperature orthorhombic form the C-N distance is 1.06 Å., the same as N-N in the iso-electronic nitrogen molecule. For sodium isocyanate, the structure of which is similar to that of sodium azide, the distances are given as C-N, 1.21 Å. and C-O, 1.13 Å. The detailed analysis of the triple halide confirms earlier work; the Cl-I and Br-I distances are 2.38 and 2.50 Å., respectively, very slightly greater in each case than the sum of the neutral radii. Linear HgCl_2 groups are also found in NH_4HgCl_3 ,⁶ which should therefore be regarded as $\text{NH}_4\text{Cl}, \text{HgCl}_2$, and in $\text{K}_2\text{HgCl}_4 \cdot 2\text{H}_2\text{O}$,⁷ the Hg-Cl distance being about 2.4 Å., although in the latter case the HgCl_2 groups deviate slightly from strict linearity. The similarity of the cell dimensions of $\text{K}_2\text{HgCl}_4 \cdot \text{H}_2\text{O}$ and $\text{K}_2\text{SnCl}_4 \cdot 2\text{H}_2\text{O}$ is probably not significant.

An accurate analysis of sodium bromate⁸ has yielded a Br-O distance of 1.78 Å.; although this is probably slightly too high (cf. I-O = 1.79 Å. in sodium periodate), previous values were undoubtedly too low. The bromine atom is displaced from the plane of the oxygens, its valency angle being 112° . The planar nature of the BO_3 group, on the other hand, has again been demonstrated in sodium metaborate⁹ and potassium pentaborate, $\text{KH}_2(\text{H}_3\text{O})_2\text{B}_5\text{O}_{10}$; ¹⁰ the latter substance contains the quinquivalent ion (I), in which the central boron atom is surrounded tetrahedrally

² H. J. Verweel and J. M. Bijvoet, *Z. Krist.*, 1938, **100**, 201.

³ M. Bassière, *Compt. rend.*, 1938, **206**, 1309.

⁴ V. Caglioti and G. Giacomello, *Ric. sci.*, 1938, **9**, 545.

⁵ (Miss) R. C. L. Mooney, *Z. Krist.*, 1938, **98**, 324.

⁶ E. J. Harmsen, *ibid.*, **100**, 208.

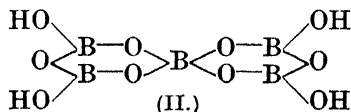
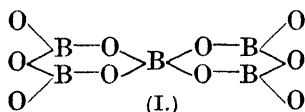
⁷ C. H. MacGillavry, J. H. De Wilde, and J. M. Bijvoet, *ibid.*, p. 212.

⁸ (Miss) J. E. Hamilton, *ibid.*, p. 104.

⁹ S. Fang, *ibid.*, **99**, 1.

¹⁰ W. H. Zachariasen, *ibid.*, 1937, **98**, 266.

by four oxygens at 1.53 Å., an appreciably greater distance than in the BO_3 triangle (1.35 Å.). The environment of the oxygen atoms not in the complex ion is considered to afford evidence that they form hydroxonium ions, but it seems doubtful whether the alternative view that they are water molecules and that the complex



ion is univalent (II) can be excluded. The ion B_3O_6 in sodium metaborate is found to have configuration and interatomic distances identical with those in the isomorphous potassium salt; it is of interest that this isomorphism results in a compromise whereby both sodium and potassium have a co-ordination number of 7 instead of the more usual 6 and 8—10 respectively.

Among substances containing AX_4 groups, accurate revisions have been made of the structures of silver permanganate,¹¹ sodium periodate,¹² and caesium chromate,¹³ while in accordance with the predictions¹⁴ of A. Strunz, durangite, $\text{NaAlF}(\text{AsO}_4)$, appears¹⁵ to be fully isostructural with titanite, $\text{CaTiO}(\text{SiO}_4)$, and olivenite, $\text{Cu}_2(\text{OH})\text{AsO}_4$,¹⁶ has the andalusite structure, containing the peculiar trigonal bipyramidal co-ordination of five oxygens to copper. The same co-ordination, although more symmetrical, occurs in the molecules of the trimethylstibine dihalides, SbMe_3X_2 .¹⁷ An unexpected discovery is the existence of square ICl_4 groups in KICl_4 ,¹⁸ with $\text{I}-\text{Cl} = 2.34$ Å., very slightly less than in $[\text{IClBr}]^-$. Since the ordinary theory of square co-ordination postulating sp^2d bonds is considered inapplicable in this case, it is suggested that this is essentially an octahedral (d^2sp^3) co-ordination with two vacant positions. In substances of the type AAlF_4 ¹⁹ ($\text{A} = \text{NH}_4$, K , Rb , or Tl), as expected, the aluminium does not form an ion AlF_4 but has the usual octahedral co-ordination which is also found in the closely related substances Tl_2AlF_5 ,²⁰ chiolite, $3\text{NaAlF}_4 \cdot 4\text{NaF}$,²¹ and cryolite, Na_3AlF_6 .²² On the other hand, the planar configur-

¹¹ K. Sasvari, *Z. Krist.*, 1938, **99**, 9.

¹² E. A. Hazlewood, *ibid.*, **98**, 439.

¹³ J. J. Miller, *ibid.*, **99**, 32.

¹⁴ See *Ann. Reports*, 1937, **34**, 164.

¹⁵ P. Kokkoros, *Z. Krist.*, 1938, **99**, 38.

¹⁶ H. Heritsch, *ibid.*, p. 466.

¹⁷ A. F. Wells, *ibid.*, p. 367.

¹⁸ (Miss) R. C. L. Mooney, *ibid.*, **98**, 377.

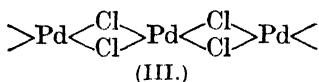
¹⁹ C. Brosset, *Z. anorg. Chem.*, 1938, **239**, 301.

²⁰ *Idem*, *ibid.*, 1937, **235**, 139.

²¹ *Idem*, *ibid.*, 1938, **238**, 201; V. Caglioti and G. Giacomello, *Naturwiss.*, 1938, **26**, 317.

²² S. von N  ray-Szab   and K. Sasvari, *Z. Krist.*, 1938, **99**, 27.

ation of auric gold is confirmed by the analysis²³ of $\text{Cs}_2\text{Au}_2\text{Cl}_6$ and $\text{Cs}_2\text{AgAuCl}_6$, which have modified perovskite structures containing square $[\text{AuCl}_4]^-$ and linear $[\text{AgCl}_2]^-$ and $[\text{AuCl}_2]^-$ ions. There is an appreciable difference between the $\text{Au}^{\text{I}}\text{-Cl}$ and $\text{Au}^{\text{III}}\text{-Cl}$ distances (2.30 and 2.42 Å., respectively). Further examples of the square co-ordination of palladium are provided by palladous chloride²⁴ and $(\text{AsMe}_3)\text{Pd}_2\text{X}_2$ ($\text{X} = \text{Cl}$ or Br);²⁵ the former is built of infinite



chains (III), in marked contrast with the rutile structure of palladous fluoride, and the same four-membered ring with almost identical angles (86° at the palla-

dium atoms) occurs in the trimethylarsine derivatives, the analysis of which affords a good example of the value of triple Fourier summations. This investigation also illustrates the difficulty of locating exactly the lighter carbon atoms on account of the swamping effect of the heavier ones; on the other hand, a recent analysis²⁶ of platinum phthalocyanine has shown that, when necessary, these difficulties can be overcome by sufficient refinement of experimental and interpretative procedure, and the results in this particular case provide some justification for the application of the Abbé diffraction theory to electron-density maps in that the effect of the first two minima and maxima around the platinum atom are clearly discernible at distances corresponding closely with those predicted by the theory.

In conclusion, attention may be directed to a useful survey of the progress of inorganic crystal chemistry during the past ten years by F. Machatschki.²⁷

E. G. C.

5. CLAY MINERALS.

Minerals based upon $(\text{Si,Al})_2\text{O}_5$ Sheets.

Micas.—Mauguin's early measurements and calculations of mica formulæ have been extended by many workers. R. E. Stevens¹ has published seventeen new chemical analyses of lepidolite, and although he does not give physical data, he marks the limits of substitution in the lithium micas. H. D. Miser² and R. E. Stevens give $\text{KLiMg}_2\text{Si}_4\text{O}_{10}\text{F}_2$ as the formula of a mineral resembling sericite from Magnet Cove, Arkansas, and identify it as the rare lithium mica taeniolite. J. Holzner³ has recalculated a number

²³ N. Elliott and L. Pauling, *J. Amer. Chem. Soc.*, 1938, **60**, 1846.

²⁴ A. F. Wells, *Z. Krist.*, 1938, **100**, 189.

²⁵ *Idem*, *Proc. Roy. Soc.*, 1938, **A**, **167**, 169.

²⁶ J. M. Robertson, private communication.

²⁷ *Naturwiss.*, 1938, **26**, 67, 86.

³ *Ibid.*, p. 104.

¹ *Amer. Min.*, 1938, **23**, 607.

² *Z. Krist.*, 1936, **95**, 435.

of mica analyses and his results, coupled with those of Stevens, show that, referred to 48 (O, OH, F) the octahedral cations total approximately 8 in muscovite, $4\text{KAl}_2\text{Si}_3\text{AlO}_{10}(\text{OH})_2$, and 12 in phlogopite, $4\text{KMg}_3\text{Si}_3\text{AlO}_{10}(\text{OH})_2$. The departures from round numbers are much more considerable for biotite and lepidolite, where the octahedral cation sum varies from 10 to 12. G. Nagelschmidt⁴ has made a study of the powder patterns of mica with a view to their identification in soil fractions, and finds that they belong to either of two types, the muscovite or the phlogopite-biotite type. Hydromuscovite,⁵ sericite, illite,⁶ the potassium-bearing clay mineral of Ross and Kerr, and Endell and Hofmann's "glimmerton" are all hydrated muscovite which cannot be distinguished with any certainty by X-ray methods from ordinary muscovite. E. Maegdefrau and U. Hofmann⁷ have also confirmed that glauconite is a mica of the muscovite type low in potassium and high in water content. Chemical analysis, specific gravity, and X-ray measurements of a hydromuscovite from Ogofau, Carmarthen-shire, show that the unit cell contains 48 (O, OH), and that replacement of oxygen by hydroxyl groups [$\text{O}_{37}(\text{OH})_{11}$ instead of $\text{O}_{40}(\text{OH})_8$] is balanced by a diminution in the potassium content from 4 to 3.88 atoms per unit cell.⁵ The departure of the ideal water content of a mica from $4\text{H}_2\text{O}$, in conjunction with the variation in atomic replacements, is probably sufficient to account for the departure from the comparatively ideal formulæ of muscovite and phlogopite of the lithium, iron, and sericitic micas. Jackson and West's analysis of muscovite still remains the only serious contribution to the crystal-structure studies of the mica family. Biotite and roscoelite, two members meriting particular attention, still await solution. A hydrated muscovite from Schmiedefeld, Thuringia, formerly determined as fine-grained pyrophyllite, contains 1.08% of V_2O_5 .⁸ It is possible that the vanadium content of the triassic red marl of the south-west of England and the Permian shales of Ölsnitz, Saxony, is due to a similar vanadium-bearing layer-structure mineral. M. Mehmel⁹ has studied the decomposition of biotite by acid, alkali, and heat treatment, using X-ray methods to identify the products, and has obtained results of interest in the investigation of sediments.

Talc and Pyrophyllite.—The structures of talc and pyrophyllite

⁴ *Z. Krist.*, 1937, **97**, 514.

⁵ A. Brammall, J. G. C. Leech, and F. A. Bannister, *Min. Mag.*, 1937, **24**, 507.

⁶ R. E. Grim, R. H. Bray, and W. F. Bradley, *Amer. Min.*, 1937, **22**, 813.

⁷ *Z. Krist.*, 1937, **98**, 31.

⁸ H. Jung, *Chem. Erde*, 1937, **11**, 38.

⁹ *Ibid.*, p. 307; *Fortschr. Min.*, 1937, **22**, autoreferate, XLVII.

have been partly confirmed by the interpretation of single-crystal photographs.¹⁰ A chemically analysed sample of the former was used. The unit cell dimensions (in Å.) are :

	Pyrophyllite, $\text{Al}_2\text{Si}_4\text{O}_{10}(\text{OH})_2$.	Talc, $\text{Mg}_3\text{Si}_4\text{O}_{10}(\text{OH})_2$.
a	5.15 ± 0.02	5.27 ± 0.02
b	8.88 ± 0.02	9.13 ± 0.03
c	18.60 ± 0.04	18.88 ± 0.05
β	$100^\circ 45' \pm 30'$	$100^\circ 15' \pm 15'$

It is found that "agreement with observed intensities is very poor and thus all structures strictly compatible with space-group requirements are eliminated as was the case for dickite." The structures are concluded to have been correctly determined by J. W. Gruner within the layer, and to be fixed along the a and c directions, but individual $[\text{Al}_2\text{Si}_4\text{O}_{10}(\text{OH})_2]_n$ or $[\text{Mg}_3\text{Si}_4\text{O}_{10}(\text{OH})_2]_n$ layers are shifted at random by some multiples of $b/6$ along the b axis.

Chlorites and Vermiculites.—Although Pauling and McMurchy's work on the chlorite family is consistent with the evidence of powder photographs, no recent single-crystal studies have confirmed the proposed structures. J. Holzner¹¹ has published chemical analyses of iron chlorites, and obtains fairly satisfactory agreement with the Pauling formulæ by calculation on a basis of 14 oxygens per unit cell. Cookeite, occurring as small curved flakes on the pegmatites of Maine, U.S.A., and at Ogofau, Carmarthenshire, probably possesses a chlorite-like structure in which the alternating talc-like and brucite-like layers are replaced by pyrophyllite-like layers $[\text{Al}_2\text{Si}_3\text{AlO}_{10}(\text{OH})_2]^1$ and lithium-bearing gibbsite layers $[\text{LiAl}_2(\text{OH})_6]^{+1}$, leading to the approximate formula $\text{LiAl}_4\text{Si}_3\text{AlO}_{10}(\text{OH})_8$. The cell dimensions determined on single crystals are $a = 5.13$, $b = 8.93$, $c \sin \beta = 28.30$ Å.⁵ One of the most interesting chlorites awaiting X-ray study is cronstedtite, the analyses of which can only be reconciled with the chlorite-type structure by including in the tetrahedral layer 4—6 ferric ions with silicon to make up the usual 16.

Gruner's structure for the vermiculites has been confirmed in the main by S. B. Hendricks and M. E. Jefferson,¹² who used single crystals of several chemically analysed specimens of vermiculite. They obtained $a = 5.33 \pm 0.05$, $b = 9.18 \pm 0.05$, $c = 28.85 \pm 0.10$ Å., $\beta = 93^\circ 15' \pm 15'$, i.e., about 4° smaller than Gruner's value. Fourier analysis of the (00 l) diffractions shows that talc-like layers are interleaved with layers of water molecules. The layers are

¹⁰ S. B. Hendricks, *Z. Krist.*, 1938, **99**, 264.

¹¹ *Neues Jahrb. Min.*, 1938, **A**, **73**, 389.

¹² *Amer. Min.*, 1938, **23**, 851.

stacked precisely as in muscovite for the a direction, but a partly random stacking of layers is found for the b direction as in talc and pyrophyllite (see above). Vermiculites form mixed structures with both the chlorites and the micas. Any mixture of mica, vermiculite, chlorite, pyrophyllite, and talc or kaolin layers might be encountered, particularly in soils. Different samples of jefferisite from Brinton's quarry, West Chester, Pennsylvania, may be either vermiculite, vermiculite-mica, or vermiculite-chlorite, so that "considerable variation can be expected even in a restricted locality." The various mixed structures may be differentiated by (1) the (00 l) spectra, (2) the swelling produced on heating, which reveals the presence of vermiculite layers. Hendricks and Jefferson also suggest that the layers of water molecules in vermiculites form hexagonal nets in which the oxygen atoms are probably coplanar. One-quarter of the hydrogen ions, *i.e.*, one hydrogen ion of alternate water molecules within the net, join the net to oxygen ions in the adjacent silicate layer. The proposed structure accounts for one-half the water being expelled from the mineral without change of the X-ray patterns.

Both J. W. Gruner¹³ and I. Fankuchen¹⁴ have studied the stilpnomelane group of minerals. Gruner, who used the powder method, interpreted his data on the basis of a monoclinic pseudo-hexagonal cell: $a = 5.23-5.27$, $b = 9.08-9.12$, $c = 12.07-12.18$ Å. Fankuchen's single-crystal measurements in Å. are :

	Orthohexagonal.			Rhombohedral.	
	a .	b .	c .	a .	a .
Stilpnomelane	22.0	38.0	37.9	17.9	76°
Ferrostilpnomelane ...	22.1	38.1	36.2	17.6	78°
Parsettensite	22.5	39.0	38.0	—	—

The Laue photographs of single flakes reveal complete asterism with hexagonal symmetry, and the character of the spots on oscillation photographs leads to a possible explanation: The 16 small pseudo-cells may vary in composition throughout the true cell and be packed not quite in perfect regularity. The structure is probably like that of chlorite, consisting of interleaved, alternate, distorted mica sheets and layers containing K, (OH), and Mg. Fankuchen's study accompanies optical, chemical and dehydration data by C. O. Hutton.¹⁴ No attempt, however, has been made to count the atoms in the unit cell; formulæ are deduced by assuming 14 (O,OH) per unit cell. No suggestion is made that one or more of these minerals have a mixed-layer structure like those found amongst the vermiculites.

Clays.—Resumés of recent work on the clay minerals include Sir

¹³ *Amer. Min.*, 1937, **22**, 912.

¹⁴ See *Min. Mag.*, 1938, **25**, 172.

William Bragg's,¹⁵ in which physical properties are shown to be closely connected with crystal-structures, W. von Engelhardt's,¹⁶ in which chemical analyses and a useful bibliography are given, and A. Brammall and J. G. C. Leech's on layer-structures and base-exchange.¹⁷ J. de Lapparent¹⁸ has classified the clay minerals in a manner running counter to the usually accepted structure work. Many problems on the mineralogy of clays await solution, and a confused nomenclature often obscures published work containing important data. In addition to papers listed in this report, additional abstracts of studies on clay minerals (other than crystal-structure analyses) are given in a special section on clays in the *Mineralogical Abstracts*.¹⁹ Abstracts of papers on clay technology are given in the *Transactions of the Ceramic Society*.

Much attention has been given to the determination of clay minerals in soils. F. A. van Baren²⁰ has made a study of changes in refractive index produced by interaction of the mineral with the immersion liquid. Von Engelhardt²¹ has described a simple method of measuring the refractive index of submicroscopic mineral particles based on measurement of the relative intensity of light scattered from a suspension of the mineral in media of various refractive indices.

Powder photographs showing marked orientation of clay minerals deposited by slow evaporation from water on to a flat surface are useful for identification.²² Mineral constituents of 2μ -soil fractions have been successfully determined by the powder method,²³ and the published photographs show that great improvements in technique have been made. The time is ripe for redeterminations of the components of other composite materials, particularly slate.

Recent work on clay minerals has been concentrated on the crystal-structure and properties of montmorillonite, the chief component of Fuller's earth²⁴ and bentonites, nontronite or chloropal, and the recently discovered magnesium-bentonite²⁵ from Hector, San Bernardino Co., California, the last being close in composition to saponite and lucianite. All these minerals

¹⁵ *Proc. Roy. Inst.*, 1938, **30**, 39.

¹⁶ *Fortschr. Min.*, 1937, **21**, 276.

¹⁷ *Science Progress*, 1937, **31**, 641; *Sci. J. Roy. Coll. Sci.*, 1937, **7**, 69; 1938, **8**, 43.

¹⁸ *Z. Krist.*, 1937, **98**, 233.

¹⁹ *Min. Abstr.*, 1938, **7**, 94.

²⁰ *Z. Krist.*, 1936, **95**, 464.

²¹ W. von Engelhardt, *Zentr. Min.*, Abt. A, 1938, 212.

²² G. L. Clark, R. E. Grim, and W. F. Bradley, *Z. Krist.*, 1937, **96**, 322.

²³ G. L. Clark, F. F. Riecken, and D. H. Reynolds, *ibid.*, p. 273.

²⁴ E. F. Newton, *Proc. Geol. Assoc.*, 1937, **48**, 175.

²⁵ W. F. Foshag and A. O. Woodford, *Amer. Min.*, 1936, **21**, 238.

give the same powder patterns but different a and b spacings (in Å.):²⁶

	Montmorillonite.	Nontronite.	Mg-bentonite.
a	5.15	5.23	5.24
b	8.95	9.11	9.16

The powder data are consistent with the structures of these minerals consisting of pyrophyllite or talc-like layers interleaved with layers of water molecules. The remarkable property of montmorillonite of shrinkage along the c direction on dehydration provides in some measure a confirmation of the proposed structure, but considerable discussion has attended the structural details, which cannot of course be decided by single-crystal work. E. Maegdefrau and U. Hofmann²⁷ find only ($hk0$) and ($00l$) diffractions on powder photographs, and conclude that the neutral $[\text{Al}_2\text{Si}_4\text{O}_{10}(\text{OH})_2]_n$ layers are stacked in parallel superposition but in random orientation about the normal to the layers. S. B. Hendricks and C. S. Ross,²⁸ however, point out that the presence of ($hk0$) reflections implies some regularity in the orientation of the layers about the layer normal and in their relative translations. These authors, from optical and electron-diffraction studies, consider that "individual montmorillonite crystals contain many aluminosilicate layers and that these layers have a rather regular arrangement with respect to one another as long as a few orders of reflection from ($00l$) can be observed."

The exact interpretation of the dehydration data of montmorillonite is also in question. G. Nagelschmidt²⁹ and, later, Maegdefrau and Hofmann²⁷ concluded that the c -spacing varies continuously as a function of the water content. W. F. Bradley, R. E. Grim and G. L. Clark,³⁰ however, regard their own data obtained by wetting dehydrated material as evidence for the existence of five hydrates containing 2, 8, 14, 20, and 26 molecules of water and with corresponding c -spacings 9.6, 12.4, 15.4, 18.4, and 21.4 Å. S. B. Hendricks and M. E. Jefferson³¹ consider that the structure of montmorillonite is made up of aluminosilicate layers (see above) interleaved with extended hexagonal nets of water molecules as in the vermiculites, and that the former layers have a relative shift with respect to one another of $n/6$ along the b direction. The distance between two neighbouring oxygen ions of the water layer is about 3.0 Å., and this spacing is considered to produce the sharp and intense diffraction on the powder

²⁶ G. Nagelschmidt, *Min. Mag.*, 1938, **25**, 140.

²⁷ *Z. Krist.*, 1937, **98**, 299.

²⁸ *Ibid.*, 1938, **100**, 251.

²⁹ *Ibid.*, 1936, **93**, 481.

³⁰ *Ibid.*, 1937, **97**, 216.

³¹ *Amer. Min.*, 1938, **23**, 863.

photographs of 3.1 Å. This proposal is more in accord with what is known of other hydrates, no close-packed arrangement of water molecules having yet been encountered. The reversible dehydration properties of montmorillonite compared with vermiculite are attributed to the very small particle size of the one mineral, and also to the presence of ions external to the pyrophyllite layers which account for the base-exchange properties of the mineral. G. Nagelschmidt and H. Z. Schofield²⁶ have produced data suggesting that the base-exchange capacities of the montmorillonite family (excluding magnesium bentonite) are closely related to the excess cations (Ca, Na, Mg, K) present. This work supports the view that a large fraction of the base-exchange cations enter into the crystal lattice and are not merely adsorbed at the surface of the particles. Sir William Bragg¹⁵ has suggested that the mechanism of base-exchange in montmorillonite takes place *via* the water molecule sheets of the structure.

Gruner's structure for dickite has now been confirmed by S. B. Hendricks,³² who reports that single crystals are piezo-electric. The stacking of layers along the *b* direction, however, is a random one, as for vermiculites, pyrophyllite, talc, and montmorillonite. Gruner's kaolinite structure is also supported by X-ray and electron-diffraction photographs by Hendricks.³³ Anauxite is supposed to have a similar structure but with vacant Al and (OH) positions; hence, the excess silica which distinguishes the mineral from kaolinite. J. W. Gruner³⁴ has measured the unit cell dimensions and specific gravities of seven chemically analysed specimens of kaolinite and anauxite. He obtains almost identical unit cell volumes but lower specific gravities for anauxite, and rejects Hendricks's conclusion, suggesting instead that tetrahedral SiO_4 groups of the tetrahedral layers are replaced by octahedral $\text{AlO}_2(\text{OH})_4$ groups. F. Machatschki,³⁵ however, refutes this structure as requiring some distortion of the anion packing, and gives an alternative solution in which six-fold and four-fold co-ordination positions (the latter being all vacant in the ideal kaolinite structure) of the $\text{Al}(\text{O},\text{OH})$ octahedral layer are statistically and partially occupied by aluminium and silicon ions respectively. Further X-ray and electron-diffraction studies have been carried out on halloysite and metahalloysite.³² The former is the fully hydrated mineral $\text{Al}_2\text{O}_3 \cdot 2\text{SiO}_2 \cdot 4\text{H}_2\text{O}$. Of Ross and Kerr's halloysite samples, 2, 8, and 9 proved to be metahalloysite, the remainder being true kaolinite. Using fully hydrated halloysite from Djebel Debar, Hendricks showed that the electron and X-ray data are consistent

³² *Amer. Min.*, 1938, **23**, 295.³³ *Z. Krist.*, 1936, **95**, 247.³⁴ *Amer. Min.*, 1937, **22**, 855.³⁵ *Ibid.*, 1938, **23**, 117.

with a structure in which neutral $[\text{Al}_2\text{Si}_2\text{O}_5(\text{OH})_4]_n$ layers are interleaved with $[(\text{H}_2\text{O})_2]_n$ layers. More recently, he has suggested³¹ that hydrated halloysite contains the extended hexagonal water molecule sheets postulated for montmorillonite and the vermiculites. There is only one layer of water molecules present between the aluminosilicate layers, however, and on dehydration the metahalloysite would be more tightly bonded between layers. This is considered to explain the irreversible character of the dehydration at 50° .³⁶

F. A. B.

6. ORGANIC STRUCTURES.

Although but few exact analyses of organic structures have been reported during the past year, much useful work continues to be done in preliminary investigations of all classes of compounds, and the value of the X-ray method in studies of semicrystalline, high-molecular substances has been shown in many publications, some of which, bearing on the structure of the proteins, are discussed in Section 7 of this Report. In the case of another high polymer, cellulose, an attempt has been made by S. T. Gross and G. L. Clark¹ to effect a definite decision between the lattices proposed by K. H. Meyer and by E. Sauter. It appears to the Reporter that the discussion on which they base their conclusion in favour of the former author's view is not sufficiently exhaustive, and that the situation still remains as summarised in last year's Report.²

Apart from X-ray investigations, various electrical and thermal measurements³ on organic compounds have furnished useful contributions to the important field of studies concerned with the relations between structure and thermodynamic properties; an interesting example of this type of work is afforded by A. R. Ubbelohde's determination⁴ of the lattice energies of some long-chain compounds, the results of which afford confirmation of A. Müller's⁵ theoretical calculations. It is very unfortunate, however, that in some investigations of long-chain compounds insufficient attention has been given to the question of purity; these substances are not readily obtained in a state of high purity,

³⁶ M. Mehmél, *Chem. Erde*, 1937, **11**, 1; *Fortschr. Min.*, 1937, **21**, 80.

¹ *Z. Krist.*, 1938, **99**, 357.

² *Ann. Reports*, 1937, **34**, 189.

³ W. O. Baker and C. P. Smyth, *J. Amer. Chem. Soc.*, 1938, **60**, 1229; A. Müller, *Proc. Roy. Soc.*, 1938, **A**, **166**, 316; A. R. Ubbelohde and J. W. H. Oldham, *Nature*, 1938, **142**, 74; J. M. Robertson and A. R. Ubbelohde, *Proc. Roy. Soc.*, 1938, **A**, **167**, 136.

⁴ *Trans. Faraday Soc.*, 1938, **34**, 282.

⁵ *Proc. Roy. Soc.*, 1936, **A**, **154**, 624.

for which neither mixed melting points nor long spacings separately are adequate criteria.⁶

Last year the similarity between the hydroxyl-bond systems of pentaerythritol and resorcinol was commented upon,⁷ and some similarity might be expected to persist in the dimorphic forms into which both are transformed at higher temperatures. This proves not to be the case, however; analysis⁸ of high-temperature (β) resorcinol shows that a rearrangement of the molecules takes place whereby a denser packing, resembling that of aromatic hydrocarbon molecules, is attained. The influence of the hydroxyl bonds thus appears to be diminished, although this is shown more by their deflection from a tetrahedral distribution than by their increase in length, which is scarcely more than the experimental error. The energy required to stretch and deflect the hydroxyl bonds is presumably more than compensated by the lower van der Waals and polarisation energies achieved in the closer packing (cf. the case of the transition ice I \rightarrow ice III⁹). The bond lengths in β -resorcinol are the same as in the low-temperature form, but the C-OH bonds are deflected out of the symmetrical position by 3° in the plane of the ring, and one of them is also deflected about 3° out of the plane. The diminution in rigidity implied by this distortion is probably not due to a large increase in thermal motion of the atoms, but may be a consequence of the molecule's being raised to an excited state at the higher temperature; in a molecule of this kind, with several possible arrangements of bonds of nearly the same energy, such an excitation is possible if it results in the new crystalline form's having lower free energy.

The transition of pentaerythritol, on the other hand, is of normal type, with increase in volume on going to the cubic high-temperature form, and although a detailed analysis has not been made, there is no doubt that rotation of all the hydroxyl groups occurs in the cubic form.¹⁰ The fact that the substance remains solid for over 70° above the transition point suggests that the rotation is of such a nature as to permit the continued existence of some kind of hydroxyl bonding.

⁶ F. Francis, F. J. E. Collins, and S. H. Piper, *Proc. Roy. Soc.*, 1937, *A*, 158, 691; S. H. Piper, *J. Soc. Chem. Ind.*, 1937, 56, 61 τ ; J. W. H. Oldham and A. R. Ubbelohde, *J.*, 1938, 201.

⁷ *Ann. Reports*, 1937, 34, 182.

⁸ J. M. Robertson and A. R. Ubbelohde, *Proc. Roy. Soc.*, 1938, *A*, 167, 122.

⁹ (Sir) W. H. Bragg, *Proc. Roy. Inst.*, 1938, 30, 283.

¹⁰ I. Nitta and T. Watanabé, *Bull. Chem. Soc. Japan*, 1938, 13, 28; C. Finbak, *Tids. Kjemi*, 1937, 17, 145; E. G. Cox and F. J. Llewellyn, unpublished.

The analysis of pentaerythritol tetra-acetate¹¹ has provided the first accurate determination of the structure of an ester group, and affords a good example of the use of triple Fourier summations.¹² All angles between single bonds in the molecule are found to be tetrahedral within experimental error, and the $\text{O}=\text{C}-\text{C}$ and $\text{O}=\text{C}-\text{O}$ angles are equal to 125° , in agreement with stereochemical theory. The bond distances are $\text{C}-\text{C} = 1.52 \text{ \AA.}$, $\text{C}-\text{O} = 1.41 \text{ \AA.}$, and $\text{C}=\text{O} = 1.33 \text{ \AA.}$; the last is appreciably greater than the value 1.24 \AA. calculated from the sum of the bond radii and found experimentally in oxalic acid dihydrate, whereas the second appears somewhat small. It may be that the $\text{C}=\text{O}$ distance is increased somewhat in ester groups, but it is difficult to see why this should be so, and it seems likely on the internal evidence that the uncertainty in bond lengths is rather greater than the amount (0.03 \AA.) assigned by the authors. The possibility of this, in a careful analysis of this kind, supports the view that the results of Fourier syntheses should, in general, be submitted to the test of structure-factor calculations with small variations in the parameters, and emphasises the very approximate nature of the bond distances given by the numerous analyses of organic compounds based on a relatively small number of qualitative intensity measurements.

In a preliminary account¹³ of the analysis of succinic acid, the interatomic distances are given as $\text{C}-\text{C} = 1.51$ and 1.52 \AA. , and $\text{C}-\text{O} = 1.28$ and 1.31 \AA. ; the conjugation present in oxalic acid no longer occurs, so that the $\text{C}-\text{C}$ distances revert to the normal single-bond length. It is noteworthy that all analyses of the last two years agree in suggesting that the pure single bond between aliphatic carbon atoms is 1.52 \AA. rather than 1.54 \AA.

Several interesting ring compounds have been examined. On account of resonance between the various possible bond arrangements, the molecule of 2:5-diketopiperazine¹⁴ is flat, with all angles in the ring 120° , and bond lengths $\text{C}-\text{O} = 1.25$, $\text{N}-\text{C}(\text{keto}) = 1.33$, $\text{N}-\text{C}(\text{methylene}) = 1.41$, and $\text{C}-\text{C} = 1.47 \text{ \AA.}$ The last two distances are unusually low, since resonance would not be expected to cause links to the methylene carbon atom to assume any double-bond character. It is probable, again, that the uncertainty in the lengths is rather greater than the 0.03 \AA. indicated by the authors, although it is notable that the $\text{N}-\text{C}(\text{methylene})$ distance in hexamethylenetetramine¹⁵ is also given as 1.42 \AA. The dimensions of the $\cdot\text{NH}\cdot\text{CO}\cdot$ group correspond closely with those found in urea.¹⁵

¹¹ T. H. Goodwin and R. Hardy, *Proc. Roy. Soc.*, 1938, A, **164**, 369.

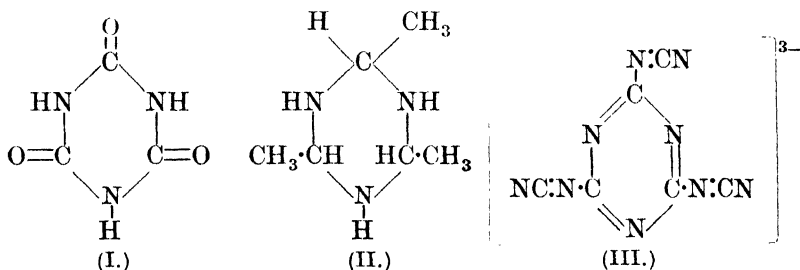
¹² *Idem*, *Phil. Mag.*, 1938, **25**, 1096.

¹³ H. J. Verweel and C. H. MacGillavry, *Nature*, 1938, **142**, 161.

¹⁴ R. B. Corey, *J. Amer. Chem. Soc.*, 1938, **60**, 1598.

¹⁵ R. W. G. Wyckoff and R. B. Corey, *Z. Krist.*, 1934, **89**, 462.

The packing of the molecules proves to be very much as suggested by J. D. Bernal;¹⁶ they are connected in long ribbons by centrosymmetrical arrangements of $\text{—NH} \dots \text{O=}$ bonds of length 2.84 Å., similar to those in isatin.¹⁷ There is no hint of any $\text{N} \dots \text{CH}_2$ interaction such as has been proposed in the case of hexamethylenetetramine.¹⁸ A somewhat similar substance is cyanuric acid, $(\text{CHON})_3$,¹⁹ whose flat six-membered ring has six equal C–N distances of 1.37 Å., unlike cyanuric triazide,²⁰ in which C–N and C= N distances of 1.38 and 1.31 Å. respectively can be distinguished. The tendency for one of the Kekulé forms to predominate is thus removed when the unsymmetrical azide group is replaced by —OH , and indeed, the mean C–O distance of 1.27 Å. suggests that the biggest contribution to the resonance structure of cyanuric acid is made by the form (I). In this crystal also there appear to be $\text{—NH} \dots \text{O=}$ bonds of about 2.8 Å. The nature of the intermolecular forces in acetaldehyde-ammonia,²¹ $\text{CH}_3\cdot\text{CHO}, \text{NH}_3$, on the other hand, is somewhat obscure. Chemical and X-ray evidence combine to show that this substance has the structure (II) + $3\text{H}_2\text{O}$ (and is the *cis*-isomer). It is suggested that



six water molecules are united by hydrogen bonds to form a puckered ring, and that the crystal is built of sandwiches of these and $(\text{CHMe}\cdot\text{NH})_3$ hexagons, held together by $\text{NH} \dots \text{H}_2\text{O}$ bonds; the length of 3.4 Å. assigned to these bonds, however, is incompatible with anything stronger than van der Waals binding. The tri-cyanomelamine ion (III) appears²² to be very similar to the iso-electronic cyanuric triazide, but accurate measurements of bond lengths are not yet available.

¹⁶ *Z. Krist.*, 1931, **78**, 363.

¹⁷ E. G. Cox, T. H. Goodwin, and (Miss) A. I. Wagstaff, *Proc. Roy. Soc.*, 1936, *A*, **157**, 399.

¹⁸ See p. 179.

¹⁹ E. H. Wiebenga and N. F. Moerman, *Z. Krist.*, 1938, **99**, 217; *Nature*, 1938, **141**, 122.

²⁰ *Ann. Reports*, 1935, **32**, 233.

²¹ N. F. Moerman, *Z. Krist.*, 1938, **98**, 447.

²² J. L. Hoard, *J. Amer. Chem. Soc.*, 1938, **60**, 1194.

X-Ray investigations of aromatic compounds are too numerous to be discussed individually; outstanding among them are the analyses of β -resorcinol (see above) and of tolan.²³ The details of the latter structure, which was mentioned briefly last year,²⁴ show that the length of the $C\equiv C$ bond is 1.19 Å., in good agreement with the value found spectroscopically in acetylene, so that the contribution of excited structures involving a double bond between the central carbon atoms is probably small. It is to be observed, however, that the electron displacement in a triple bond may be enough to cause the X-ray value for its length to be slightly shorter than the same bond measured spectroscopically, since in the latter case the internuclear distance is determined. The C-C bonds connecting the central atoms to the benzene rings are only 1.40 Å., as compared with 1.44 Å. in stilbene; this contraction in a single bond adjacent to a triple one is difficult to account for in terms of resonance, although an explanation of another kind can probably be given.²⁵ A similar contraction is found spectroscopically in several acetylene derivatives. A somewhat different case, for which no theoretical explanation is available, is the short C-CH₃ distance (1.47 Å.) in durene,²⁶ and it is interesting to note that a revision²⁷ of the structure of hexamethylbenzene, in which the same distance can be measured more accurately, yields the value 1.53 Å.

E. G. C.

7. PROTEINS.

For the purposes of summarising recent developments in the X-ray study of protein structure, a more convenient introduction could hardly be found than T. W. J. Taylor's Report last year¹ on "The Chemistry of Proteins and Related Substances." The present section may be considered as being a crystallographic continuation of that report.

A simple, and perhaps not altogether surprising, generalisation seems to have been reached in the X-ray classification of the fibrous proteins,² in that they all appear to fall into no more than two main groups, the keratin-myosin group (including its β -sub-group) and

²³ J. M. Robertson and (Miss) I. Woodward, *Proc. Roy. Soc.*, 1938, A, **164**, 436.

²⁴ *Ann. Reports*, 1937, **34**, 187; cf. J. M. Robertson, *J.*, 1938, 131.

²⁵ W. G. Penney and G. J. Kynch, *Proc. Roy. Soc.*, 1938, A, **164**, 409.

²⁶ J. M. Robertson, *ibid.*, 1933, A, **142**, 659.

²⁷ *Idem*, *J. Soc. Chem. Ind.*, 1938, **57**, 1056.

¹ *Ann. Reports*, 1937, **34**, 302.

² W. T. Astbury, *Compt. rend. Trav. Lab. Carlsberg* (Sørensen Jubilee Vol.), 1938, **22**, 45; *Trans. Faraday Soc.*, 1938, **34**, 377; *Kolloid-Z.*, 1938, **83**, 130.

the collagen group. The normal state of the former group is that of the regularly-folded α -form, but this may be converted into the fully-extended β -form by stretching or by means, of the type of denaturation, which also serve to disrupt the intramolecular folds. The chief muscle protein, myosin,^{2,3} turns out to be extraordinarily like the hair protein, keratin, in its labile or "supercontracting" form, i.e., when the disulphide bridges so characteristic of the keratins have been largely broken down,⁴ both as regards molecular configuration and elastic properties; and the conclusion has been drawn that the contraction of muscle is the consequence of a further folding of the α -form of myosin analogous to the supercontraction of keratin.

The keratin-myosin group includes also the fibrous proteins of the epidermis⁵ and probably those of myo-epithelial tissue too.³ It undoubtedly connotes something very fundamental in the make-up of living things, some configuration that, suitably graded in sensitivity by modifications introduced during differentiation, must be used widely as the basis of long-range elasticity. An extreme modification used by birds and reptiles, as opposed to mammals (which use α -keratin), is "feather keratin," which occurs in a slightly constricted β -configuration.⁶

Outside the keratin-myosin group all, or almost all, other natural protein fibres fall into the collagen group, which includes such structures as connective tissue, tendons, cartilage, elastoidin,⁷ etc. Fibres of the collagen group (except elastin) exist normally in what appears to be a stereochemically fully-extended configuration—not the *trans*-configuration of the β -proteins, but perhaps a *cis*-configuration⁸—but they contract strongly in hot water at rather specific temperatures. The contracted form then shows long-range elasticity like that of the keratin-myosin group, and this property, taken into consideration with the X-ray photographs,^{7,2} makes it clear that once more we must postulate the folding and unfolding

³ W. T. Astbury and S. Dickinson, "X-Ray Studies of the Molecular Structure of Muscle" (in preparation).

⁴ J. B. Speakman, *Nature*, 1933, **132**, 930; 1936, **138**, 327; *J. Text. Inst.*, 1936, **27**, P231.

⁵ K. M. Rudall, Ph.D. Thesis, Leeds, 1936; A. Giroud and G. Champetier, *Bull. Soc. Chim. biol.*, 1936, **18**, 656; J. C. Derksen and G. C. Heringa, *Polska Gaz. lekarska*, Szymonowicz Festschr., 1936, **15**, 532; J. C. Derksen, G. C. Heringa, and A. Weidinger, *Acta Neerland. Morph.*, 1937, **1**, 31.

⁶ W. T. Astbury and T. C. Marwick, *Nature*, 1932, **130**, 309; W. T. Astbury, *Trans. Faraday Soc.*, 1933, **29**, 193; *Kolloid-Z.*, 1934, **69**, 340; *Chem. Weekblad*, 1936, **33**, 778.

⁷ W. T. Astbury and R. Lomax, *J.*, 1935, 846; G. Champetier and E. Fauré-Fremiet, *J. Chim. physique*, 1937, **34**, 197.

⁸ W. T. Astbury, *Chem. Weekblad*, 1936, **33**, 778.

of polypeptide chains. The highly elastic protein of the *ligamentum nuchae*, elastin, apparently gives the collagen fibre photograph only on stretching,⁹ from which it is a fair conclusion that elastin is a member of the collagen group characterised by a thermal-transformation temperature below ordinary temperatures.²

The fact that, according to X-rays, all the fibrous proteins fall into two, or very few, main configurational groups provides still another argument against perpetuating any real distinction between "fibrous" and "globular" proteins; for one of the implications of the results obtained by T. Svedberg and his collaborators with the ultra-centrifuge is surely that in the whole of the protein field only a few configurations are used out of the enormous number of theoretical possibilities. A similar inference may be drawn from the recent results of M. Bergmann and C. Niemann,^{9a} which show also—and this is supported by X-ray data¹—that the Svedberg generalisation of multiple molecular weights, deduced from the study of "globular" proteins, holds for fibrous proteins too. More impressive still, however, is this, that within one and the same configurational group of the fibrous proteins there are wide variations in chemical constitution like those found between members of each of Svedberg's molecular-weight groups.¹⁰

That there are great variations of molecular shape within each of the various molecular-weight groups is also evident from T. Svedberg's data:¹¹ indeed, X-rays indicate that the range of variation includes even the fully-extended, or β -, proteins.^{1, 12} In proteins *as we know them now*, configuration is not decided by strict chemical constitution, and neither shape nor chemical constitution is the chief factor in fixing molecular weight. The apparent conflict between chemical constitution and configuration may be resolved, nevertheless, by some such concept as unifies the aromatic compounds, which are all based on the benzene ring and its homologues.

Similar intramolecular folds are probably used in the structure of both fibrous and globular proteins, but their precise nature still eludes us, though crystallographic cell dimensions, number of molecules per cell, molecular weight, and in some cases space-group also, have been worked out for the following globular proteins:

⁹ H. Kolpak, *Kolloid-Z.*, 1935, **73**, 129.

^{9a} *J. Biol. Chem.*, 1936, **115**, 77; 1937, **118**, 301.

¹⁰ W. T. Astbury, Royal Society Discussion on Protein Structure, Nov., 1938.

¹¹ *Nature*, 1937, **139**, 1051; *Ind. Eng. Chem.*, 1938, **10**, 113.

¹² W. T. Astbury and F. O. Bell, Cold Spring Harbor Symposia on Quantitative Biology, 1938, **6**.

insulin,¹³ excelsin,^{14, 15} lactoglobulin,¹⁶ chymotrypsin,¹⁷ hæmoglobin,¹⁷ pepsin,¹⁸ and tobacco-seed globulin.¹⁹ Insulin has also been submitted to a Patterson analysis,¹³ but the interpretation for the present is under discussion. D. M. Wrinch²⁰ argues that the correct solution is the cage-like structure she had proposed for both insulin²¹ and pepsin.²² This structure, the "C₂ cyclol," besides being of the right sort of shape for insulin and pepsin, is built from 288 residues and therefore offers a very striking geometrical explanation of the Svedberg 35,000 group and the findings of M. Bergmann and C. Niemann; but it is difficult to reconcile it with the great variations in shape within the group, and with the evidence that the larger protein molecules are formed by the union of relatively small sub-units, all of a similar density and probably of a fibrous nature.¹²

The liberation of polypeptide chains when globular proteins form monolayers has now been placed beyond doubt.^{23, 12} Multi-layers prepared by the technique of I. Langmuir and K. Blodgett,²⁴ and consisting of up to 1764 monolayers of egg albumin, have been detached from their metal base and examined mechanically, optically, and by X-rays. The conclusion is that such multilayers of egg albumin consist of polypeptide chains roughly oriented in the direction of movement of the slide, and laid down with their side chains approximately perpendicular to the surface. The side-chain spacing is about $9\frac{1}{2}$ Å., agreeing closely with the thickness per monolayer given by direct measurement of the multilayer thickness, which was obtained first by means of an optical arrangement independent of the optical constants of the films themselves, and then even by means of an ordinary screw micrometer! E. Stenhagen²⁵ has since obtained similar results from 40 layers of a

¹³ (Miss) D. Crowfoot, *Nature*, 1935, **135**, 591; *Proc. Roy. Soc.*, 1938, *A*, **164**, 580.

¹⁴ W. T. Astbury, S. Dickinson, and K. Bailey, *Biochem. J.*, 1935, **29**, 2351.

¹⁵ W. T. Astbury, S. Dickinson, and F. O. Bell, unpublished results.

¹⁶ (Miss) D. Crowfoot and D. Riley, *Nature*, 1938, **141**, 521.

¹⁷ J. D. Bernal, I. Fankuchen, and M. Perutz, *ibid.*, p. 521.

¹⁸ J. D. Bernal and (Miss) D. Crowfoot, *ibid.*, 1934, **133**, 794.

¹⁹ (Miss) D. Crowfoot and I. Fankuchen, *ibid.*, 1938, **141**, 521.

²⁰ *J. Amer. Chem. Soc.*, 1938, **60**, 2005; *Nature*, 1938, **142**, 955; D. M. Wrinch and I. Langmuir, *J. Amer. Chem. Soc.*, 1938, **60**, 2247; *Nature*, 1938, **142**, 581; E. H. Neville, *ibid.*, p. 994.

²¹ D. M. Wrinch, *Trans. Faraday Soc.*, 1937, **33**, 1368.

²² *Idem*, *Phil. Mag.*, 1937, **24**, 940.

²³ W. T. Astbury, F. O. Bell, E. Gouter, and J. van Ormondt, *Nature*, 1938, **142**, 33.

²⁴ K. M. Blodgett, *J. Amer. Chem. Soc.*, 1935, **57**, 1007; I. Langmuir, V. J. Schaefer, and D. M. Wrinch, *Science*, 1937, **85**, 76.

²⁵ *Trans. Faraday Soc.*, 1938, **34**, 1328.

lipo-protein photographed with the condensing monochromator designed by I. Fankuchen.²⁶

The most far-reaching protein discovery for years is that of the nature of the tobacco mosaic and related viruses, which have been found to be chemical individuals of the nucleo-protein class. X-Ray examinations have been carried out by R. W. G. Wyckoff²⁷ and J. D. Bernal²⁸ and their collaborators, but mostly by the latter group, who have made an intensive study of three strains of tobacco virus and two of cucumber virus. The units in pure preparations of these are apparently * rod-like bodies about 150 Å. thick when dry. All the preparations, except the most dilute solutions, are actually liquid-crystalline: the rods fit together laterally in two-dimensional hexagonal close packing, but have no regularity of packing in the direction of their length. The X-ray pattern is composite, one part—the *intramolecular* pattern—being a fibre diagram that remains practically unchanged in all preparations from solutions up to the dry gel, and the other—the *intermolecular* pattern—a system of side reflections whose spacings vary with the proportion of water present. The lateral separation of the rods is increased to about 210 Å. in the wet gel, and to as much as 450 Å. in a 13% solution, and all the while the particles remain distributed uniformly in a two-dimensional hexagonal arrangement!

The intramolecular pattern, which repeats along the fibre axis at intervals of about 69 Å., shows, of course, that the giant molecules are built up from sub-units that are relatively small. J. D. Bernal³¹ now favours a sub-unit of dimensions about $11 \times 10 \times 10$ Å., but he originally suggested $22 \times 20 \times 20$ Å.²⁸ It can be shown,³² however, from the nucleic acid content (5%) and X-ray data on the proteins and nucleic acids^{33, 12} (see below) that the larger dimensions correspond at any rate to the smallest possible *chemical*

²⁶ *Nature*, 1937, **139**, 193; *Physical Rev.*, 1938, **53**, 909.

²⁷ R. W. G. Wyckoff and R. B. Corey, *J. Biol. Chem.*, 1936, **116**, 51.

²⁸ F. C. Bawden, N. W. Pirie, J. D. Bernal, and I. Fankuchen, *Nature*, 1936, **138**, 1051; J. D. Bernal and I. Fankuchen, *ibid.*, 1937, **139**, 923.

²⁹ H. S. Loring, M. A. Lauffer, W. M. Stanley, F. C. Bawden, N. W. Pirie, K. M. Smith, and W. D. MacClement, *ibid.*, 1938, **142**, 841.

³⁰ J. D. Bernal, I. Fankuchen, and D. P. Riley, *ibid.*, p. 1075.

³¹ Private communication.

³² W. T. Astbury and W. M. Stanley, Discussion on Stanley's paper at Cold Spring Harbor Symposium, 1938.

³³ W. T. Astbury and F. O. Bell, *Nature*, 1938, **141**, 747.

* There is some disagreement²⁹ as to whether the true unit is really rod-shaped: there is evidence that it may be almost round like that of the tomato "bushy-stunt" virus, but is aggregated into rods by the methods of isolation. Bushy-stunt virus crystallises in rhombic dodecahedra and gives X-ray photographs corresponding to a body-centred cubic lattice.³⁰

sub-unit, for the volume they include is associated with just one nucleotide, in combination with about 54 amino-acid residues.

The dimensional data on the nucleic acids have been obtained principally from an X-ray study of thymonucleic acid and its compound with clupein.^{33, 12} The unit in pure preparations of sodium thymonucleate, the viscous solutions of which show streaming double refraction,³⁴ appears to be a column of some 2,000 flat, or flattish, nucleotides piled on top of one another at 3.3_4 A. apart. This distance is almost exactly equal to the spacing of the side chains in a fully-extended polypeptide, with the result that clupein, for instance, a simple polypeptide of about 28 residues, 21 of which are arginine residues,³⁵ combines readily with thymonucleic acid to form a fibrous compound that gives an X-ray photograph remarkably like that of the sodium compound: the outstanding period along the fibre axis of 3.3_4 A. remains unchanged. The fibres of clupein thymonucleate are optically negative with respect to their length, just as are the nucleic acid-containing³⁶ bands of the salivary chromosomes with respect to the chromosome length,³⁷ from which it may be inferred that if the protamine-thymonucleic acid compounds in the chromosomes are similar to clupein thymonucleate, then the protein chains must run along their length. Thus for the first time we arrive *experimentally* at a reasonable molecular basis for the physicochemical properties of the chromosomes and their linear genic pattern; for protein chains, perhaps modulated by combination with nucleic acid, are naturally what we first think of as likely bearers of such properties.

W. T. A.

W. T. ASTBURY.

F. A. BANNISTER.

A. J. BRADLEY.

E. G. COX.

³⁴ R. Signer, T. Caspersson, and E. Hammarsten, *Nature*, 1938, **141**, 122.

³⁵ K. Linderström-Lang, *Trans. Faraday Soc.*, 1935, **31**, 324; K. Linderström-Lang and K. E. Rasmussen, *Compt. rend. Trav. Lab. Carlsberg*, 1935, **20**, 1.

³⁶ T. Caspersson, *Skand. Arch. Physiol.*, 1936, **73**, Suppl. No. 8.

³⁷ W. J. Schmidt, *Naturwiss.*, 1937, **25**, 506.

ORGANIC CHEMISTRY.

I. INTRODUCTION.

THE study of the mechanisms of chemical reactions, which has not received much attention in recent Reports, continues to provide a fruitful field of research, and our knowledge of many changes in which organic compounds participate has been enriched by the results of a large number of recent investigations. In the present Report the policy of presenting certain topics with a reasonable amount of detail has been adopted and the consideration of much important work is postponed until a future occasion. A series of kinetic studies of replacements in aliphatic compounds have shown that in the reaction $Z + RX \longrightarrow RZ + X$ (e.g., $OH' + RCl \longrightarrow ROH + Cl'$), the removal of the group X and the addition of Z may occur either simultaneously ("bimolecular mechanism") or consecutively ("unimolecular mechanism"). The predominance of one mechanism or the other is conditioned, *inter alia*, by the nature of R and of the medium. The examination of a number of replacements at an asymmetric carbon atom under kinetically controlled conditions has thrown light upon much that was obscure in connection with the Walden inversion; the steric course of the substitution depends largely upon its mechanism. Olefin elimination from alkyl halides and other compounds may proceed by a "bimolecular" or by a "unimolecular" mechanism, and similar possibilities have been demonstrated in anionotropic and allied changes. The investigation of prototropic systems has been continued; this has included the measurement of speeds of isomerisation, halogenation, racemisation and deuterium exchange. The introduction of deuterium into the aromatic nucleus follows the ordinary substitution rules.

The general problem of the influence of substituent groups upon reactions has been approached from two points of view: (a) by the analysis of reaction velocities on the basis of the kinetic equation, $k = PZe^{-E/RT}$, and (b) by the interpretation of chemical and physicochemical data in the light of permanent and time-variable electronic effects, each operating by two distinct mechanisms. Halogens and alkyl groups present peculiar features, as also, of course, do groups standing in the ortho-positions in aromatic compounds, and efforts have been made to trace the origin of these peculiarities.

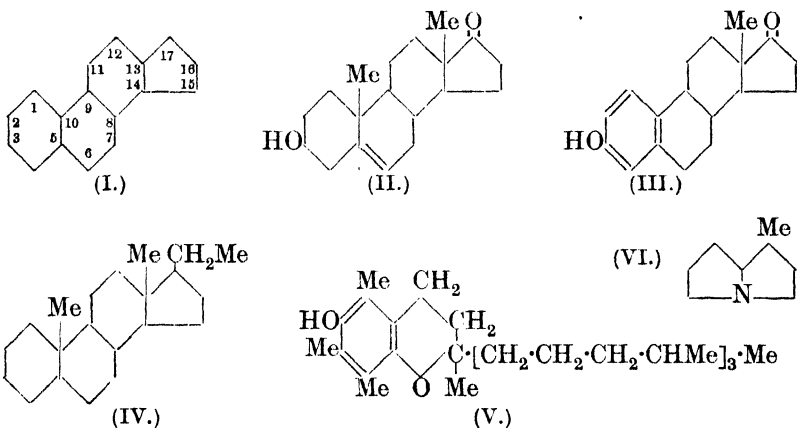
The aim of the Report on fatty acids and other long-chain compounds is to present to the organic chemist an account of the advances in our knowledge of the structure of higher aliphatic compounds arising out of studies of crystallisation and melting. Some of the developments have been treated separately in earlier Reports, but in view of the complementary nature of the researches it appeared worth while to attempt a general survey. As in some of the topics there are at least fifteen years' publications to be reviewed, it will not be possible this year to deal with purely chemical work on higher aliphatic compounds, except for a few methods of preparation. The main departure from the earlier work in this field is the recognition that very different criteria of purity must be applied in dealing with higher aliphatic compounds from those found sufficient for lower aliphatic or for aromatic substances. Binary systems from pure homologues have thrown light on the behaviour of naturally occurring mixtures and have brought out the analogy between liquid crystals and some forms of aliphatic compounds. The crystal structure of long-chain compounds has been made fairly clear by X-ray methods; X-ray analysis of films is also used for identification of pure compounds and for confirmation of the results of other methods of analysing mixtures. There have been many contributions to the study of polymorphism, alternation of melting points in homologous series, and compound formation.

Many advances have been made in the chemistry of the terpenes since they were last reviewed in these Reports for 1935. Interesting syntheses have been effected in the monoterpene group. The abnormal rearrangement of the isoprene residues in *Artemesia* ketone has been confirmed by the synthesis of the tetrahydro-derivative. Thujane has been prepared from *l*-menthone and also from a cyclopentene derivative, and the cyclopropane nature of the thujane group is established by the synthesis of umbellularic acid, a degradation product of umbellulone. Carane has been prepared from a cyclohexene derivative, syntheses of verbanone, δ -pinene and pinane from cyclobutane derivatives have been described and fenchone has been obtained from camphenonic acid. New investigations have removed several difficulties from camphor chemistry. For instance, oxidation of α -campholenic acid yields α -campholonic, and not pinonic acid as previously reported, more attractive structures have been suggested for sulphocamphylic and the related camphylic acids, and a study of camphenyl chloride and camphenylene shows that the constitution of the latter, put forward on Raman spectra evidence, is inconsistent with degradation experiments. Two different syntheses of ketones, probably structurally identical with the cyperones, indicate

that these sesquiterpene ketones are of the eudalene type, derived from head-to-tail union of three isoprene units. Researches on eremophilone have led to the conclusion that the structure cannot be based on the skeleton of 1:9-dimethyl-7-isopropyldecalin; two alternatives have been suggested, but a final solution of the problem has not been made. The constitution of the caryophyllenes is still uncertain; a structure advanced some years ago is disproved by the synthesis of homocaryophyllenic acid and a new structure containing a fusion of four- and seven-membered rings has been suggested. New alcohols, known as the betulenols, have been investigated and a relationship between these compounds and the caryophyllenes has been established. A novel structure containing a *cyclopentene* ring has been tentatively advanced for the sesquiterpene alcohol, lanceol, and it is worthy of note that the *cyclopentene* system is present in the naturally occurring ketone, jasmone, $C_{11}H_{16}O$. The constitution of ledol has been amended on the grounds of its relationship to the azulenes, and the structure of irene, an important degradation product of irone, has been confirmed synthetically.

The term "steroid" is employed as a generic term for the natural products, including the sterols, bile acids, heart poisons, saponins and sex hormones, which are characterised by the common skeleton (I), and the undiminished activity in this field justifies a further report on the chemistry of these substances. Most of the work during the last two years has been stimulated by discoveries in the group of steroidal sex hormones, which have the physiological activities characteristic of the gonads. Removal of the side chain from the sterols is now effected on a manufacturing scale and investigations have been directed towards the production, from androstane intermediates, *e.g.*, *trans*-dehydroandrosterone (II), of more active substances such as testosterone (the most active male natural hormone) or compounds of therapeutic advantage. The preparation of compounds of protracted physiological activity has received attention and other investigations on the bromination and subsequent dehalogenation of the steroids have led to unsaturated compounds showing both oestrogenic and androgenic activity. The possibility of transition from one group of hormones to another has been examined. A route to the oestrone (III) series either from androstane intermediates or from sterols (by removal of the 17-side chain after aromatisation of ring I) has been opened. The pregnane (IV) series includes progesterone, the hormone of the corpus luteum of the ovary, and the "life maintenance" hormone of the adrenal cortex. It seems less practicable to obtain these important but inaccessible substances by arresting the degradation of the sterol side

chain, than to synthesise them from 17-ketoandrostane derivatives, and reactions of the latter type are being examined. Of the new natural products which have been isolated, the adrenal cortical steroids are most important. The investigations of T. Reichstein, including the analysis of complex tissue extracts, the separation of the highly active corticosterone, the artificial preparation and later the isolation of deoxycorticosterone, and the elucidation of the constitution of the compounds, form a remarkable chapter in the chemistry of natural products. Of the structural questions which arise, one of importance concerns the position of an inert oxygen atom, investigation into which has had repercussions in the heart poison group. The steroids of urine are now recognised as trans-



formation products of the body steroids, and much new work in this field has been done, but neither the biochemical nor the structural problems can be regarded as settled. The "Vitamin D problem" is still not completely solved on the structural side. On the biological side it now appears that the precursors are either ergosterol or 7-dehydrocholesterol, and calciferol and "vitamin D₃" the corresponding natural antirachitic vitamins.

In recent years developments in the heterocyclic division have centred around natural products, particularly those of pronounced physiological activity. The isolation in 1936 of α -tocopherol with vitamin E activity and the inevitable concentration of research in this field led to an amazingly rapid solution of the structural problem. Progress has been made in other directions and several topics which have been developing steadily are reviewed in the present Report. Dioxan, discovered in 1907, has recently come into prominence as a solvent useful both for cryoscopic determinations and as a medium for organic reactions, and an addition product with sulphur trioxide has

been advocated as a sulphonating agent. α -Tocopherol has been synthesised from ψ -cumoquinol and phytol. The synthesis is ambiguous, but the degradation evidence favours the phenolic chroman (V) and not the alternative coumaran structure. The structure of equol, a phenol isolated from horse urine, has been limited to alternative coumaran or chroman formulæ. The effect of alkali on *Derris* constituents has been examined, an important advance has been made in the chemistry of rottlerin, the structure of which is now limited to one of two chromen formulæ, and a novel structure containing a ring composed of one oxygen atom and nine carbon atoms has been advanced for usnic acid. The observation that high-temperature bromination of 2 : 2'-dipyridyl leads to substitution in the α -positions has been used in preparing and establishing the structures of a series of polypyridyls. Important improvements have been discovered in the preparation of glyoxalines and benz-*iminazoles*, and a new type of heterocyclic compound has been prepared from *o*-phenylenediamine and glucose. The bacterial pigments oxychlororaphine, pyocyanine and the pigment of *Chromobacterium iodinum* contain the phenazine nucleus and syntheses of the first two have been described. Important contributions to phenazine chemistry have been made, including the isolation of crystalline phenazyl radicals. An examination of the American species of *Dicentra* and *Corydalis* has revealed the presence of thirty alkaloids hitherto undiscovered in the Asiatic plants, and the isolation of some new bases of the narcotine type is noteworthy. The constitution of the bis-*isoquinoline* alkaloid, cepharanthin, has been limited to two formulæ. A relationship has been discovered between alkaloids of the *Senecio* and the *Heliotropium* species; on hydrolysis the alkaloids give acids of unknown structure and one of three C_8 bases, all of which yield the same reduction product of structure (VI).

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F. B. KIPPING.
J. C. SMITH.
H. B. WATSON.

2. REACTION MECHANISMS.

The classification of reagents as "negative-centre seeking" and "positive-centre seeking" is a very old one, and the terms "kationoid" and "anionoid" have been used by Lapworth and others to describe these two types. Since, however, the classification depends solely upon the affinity of the reagent for electrons or for

nuclei, independently of its state of electrification, the nomenclature "electrophilic" and "nucleophilic" has been suggested by C. K. Ingold¹ as more appropriate. An electrophilic reagent is defined as one which acquires electrons or a share in electrons belonging to some other atom or ion, and a nucleophilic reagent as one which transfers electrons to or shares its electrons with a foreign nucleus.

It is evident that when an electrophilic reagent attacks a molecule it will do so at a point where the electron density is high relatively to the nuclear field; moreover, the greater the electron density (relatively to the field), the more facile the reaction. Common electrophilic reagents are those which bring about the replacement of hydrogen of the aromatic nucleus (hence the *op*-orientation and the facility of substitution when an electron-releasing group such as $-\text{O}\cdot\text{CH}_3$ is present) or add at olefinic linkages (where electron-repulsive groups cause increased speed).² A nucleophilic reagent, on the other hand, seeks a point of low electron density (again relatively to the nuclear field), and the greater the deficiency of electrons the more rapid the reaction. Nucleophilic reagents include the hydroxyl ion (as in alkaline hydrolyses which are normally favoured by electron-attractive groups) and the reagents which add at carbonyl carbon (*e.g.*, in $>\text{CO} + \text{CN}' \longrightarrow >\text{C}(\text{CN})\cdot\text{O}'$, the first step in cyanohydrin formation). Acids, defined in the Lowry-Brönsted generalised sense as proton donators, and oxidising agents (electron acceptors) are included in the larger class of electrophilic reagents, and bases (again defined in the generalised manner) and reducing agents (which donate electrons) are similarly included in the class of nucleophilic reagents.

Whereas electrophilic reagents seek the most negative, and nucleophilic reagents the most positive point of a molecule, a number of instances have been observed in which *either* of these points may be attacked. One criterion of this type of reaction is that substitution in an aromatic compound is always *op*, whether the directing group be of the *op*-type (when normally all positions are negative but the *o*- and *p*- are the *most* negative) or of the *m*-directive type (when all positions are positive but the *o*- and *p*- are *most* positive). The actual substituting reagent is here a free neutral organic radical (produced by the *symmetrical* rupture of a covalent bond);³ reference was made in last year's Report to the reactions of these radicals in the liquid phase.⁴ The incompleteness

¹ J., 1933, 1120; *Chem. Reviews*, 1934, **15**, 225.

² C. K. Ingold and (Mrs.) E. H. Ingold, J., 1931, 2354.

³ D. H. Hey and W. A. Waters, *Chem. Reviews*, 1937, **21**, 169.

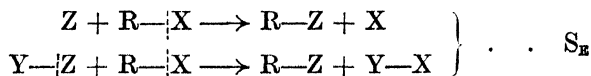
⁴ *Ann. Reports*, 1937, **34**, 282.

of the octet of one carbon atom renders the radical an electrophilic reagent, and the presence of an unshared electron renders it nucleophilic; it thus combines the properties of the two common types of reagent.⁵ The similarity of the behaviour of neutral radicals in solution to that of radicals in the gas phase has now been demonstrated further, and their reactions have been applied to the preparation of a number of derivatives of diphenyl and *p*-terphenyl,⁶ and also of aromatic compounds of antimony and tellurium; reaction occurs less readily or not at all with non-metallic elements such as sulphur, selenium, phosphorus, boron, carbon and silicon.⁷

In striking contrast with aromatic substitution, which has been the subject of a multitude of researches during several decades, substitution at a saturated carbon atom has received relatively little attention until recently. In the past few years, however, the investigation of aliphatic substitution has made very substantial progress, and the knowledge so gained has thrown much light upon the phenomenon of optical inversion. This work is summarised in the paragraphs which follow, and some of the recent researches upon prototropic and anionotropic systems are then dealt with. A somewhat arbitrary selection of topics has resulted in the omission of reference to much of the recent work upon reaction mechanisms, and this shortcoming is illustrated by the absence of any consideration of intramolecular rearrangements or of the Kharasch peroxide effect. Any attempt to review the whole field in one Report would inevitably have reduced this section to a mere catalogue of the more important researches, however, and of the two evils the former has been preferred.

Aliphatic Substitution.—The term “substitution” is here used to designate the replacement of *any* group by any other. Substitution by electrophilic and by nucleophilic reagents may be represented by the following general schemes, which refer to cases where the reaction involves the rupture either of one bond (“three-centre system”) or of two (“four-centre system”):

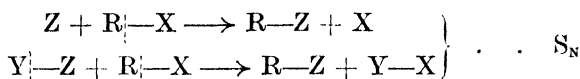
Electrophilic Substitution



⁵ C. K. Ingold, *Chem. and Ind.*, 1937, 57, 112.

⁶ W. S. M. Grieve and D. H. Hey, *J.*, 1938, 108; I. M. Heilbron, D. H. Hey, and R. Wilkinson, *ibid.*, pp. 113, 699; E. C. Butterworth and D. H. Hey, *ibid.*, p. 116; H. France, I. M. Heilbron, and D. H. Hey, *ibid.*, p. 1364; E. C. Butterworth, I. M. Heilbron, D. H. Hey, and R. Wilkinson, *ibid.*, p. 1386.

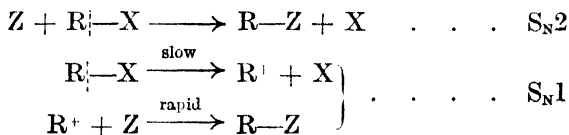
⁷ F. B. Makin and W. A. Waters, *ibid.*, p. 843; W. A. Waters, *ibid.*, p. 1077.

Nucleophilic Substitution

(The dotted lines indicate the fate of the electron pairs originally forming the covalent bonds which are broken.)

In a comprehensive discussion of substitution processes in solution, E. D. Hughes and C. K. Ingold⁸ have suggested that reactions of any of these types may proceed by either of two mechanisms, which they name the "bimolecular" ($\text{S}_{\text{E}}2$; $\text{S}_{\text{N}}2$) and "unimolecular" ($\text{S}_{\text{E}}1$; $\text{S}_{\text{N}}1$) mechanisms. Substitution requires the addition of one group and the removal of another, and in a bimolecular process these steps are now regarded as proceeding simultaneously;⁹ the formation of the transition complex involves the bringing up of the reagent and the stretching of the bond which is ultimately to be ruptured. Hughes and Ingold visualise an alternative mechanism of substitution, however. If the group which is to be replaced is not bound too strongly, solvation may reduce the energy of ionisation by an amount comparable in magnitude with the bond strength,* and a rupture of the bond at measurable speed may precede an almost instantaneous reaction of the ion with the attacking reagent, *i.e.*, bond fission and bond formation may be separated into stages, of which the former controls the rate. Such a mechanism is not possible when the group is held very firmly, as is the case with groups linked to the aromatic nucleus, and the theory applies essentially to substitution at a saturated carbon atom and in solution. Ingold, Hughes, and their collaborators have carried out extensive studies of nucleophilic substitutions of this type.¹⁰

For cases where one bond is broken the two mechanisms of nucleophilic substitution are formulated :



It is evident that reactions occurring by these mechanisms will be bimolecular ($\text{S}_{\text{N}}2$) and unimolecular ($\text{S}_{\text{N}}1$) respectively. Mechanism $\text{S}_{\text{N}}1$ will be favoured relatively to $\text{S}_{\text{N}}2$ by large electron release from R, strong electron-affinity in X, low nucleophilic

⁸ *J.*, 1935, 244

⁹ F. London, *Z. Elektrochem.*, 1929, **35**, 552.

¹⁰ See summary by E. D. Hughes, *Trans. Faraday Soc.*, 1938, **34**, 185.

* This answers the objection that an ionisation mechanism would involve too great an energy of activation (A. R. Olson and H. H. Voge, *J. Amer. Chem. Soc.*, 1934, **56**, 1690).

activity (basicity) and low concentration of the reagent Z, and high ionising capacity of the solvent. The corresponding mechanisms for electrophilic substitution (S_E2 and S_E1) and the factors favouring mechanism S_E1 may be deduced similarly.

The new experimental evidence which is put forward in favour of the view outlined above relates to the degradations of 'onium salts and the hydrolysis of alkyl halides; Hughes and Ingold further quote various observations from the literature which are in accord with their views. If the group R be varied in the direction of increasing electron release, the effect will be to oppose the attack of the nucleophilic reagent which is necessary for mechanism S_N2 , and to facilitate the ionisation which is the rate-determining step in mechanism S_N1 ; a sufficiently large range of variation in the electron-repulsion by R would be expected to lead first to a retardation of the reaction by mechanism S_N2 , and then to a change of mechanism to S_N1 , followed by an *increase* of speed (this reversal of the effect of electron-repulsion is due, of course, to the fact that in mechanism S_N1 the nucleophilic reagent Z is not attacking the molecule itself, and the measured speed is that of an ionisation which is facilitated by a flow of electrons from R). There will thus be a mechanistic critical point, on either side of which one mechanism predominates, and, except in the neighbourhood of this point, reaction by the other mechanism will be almost negligible. While, however, increasing electron release by the group R will lead to diminishing velocity in the region where mechanism S_N2 operates, the observed retardation may be small or even irregular, since an increasing opposition to the approach of the reagent (process *a* below) is to some extent counteracted by an increased facility in the

expulsion of the group replaced (process *b*); $Z \overset{\curvearrowright}{\text{---}} R \text{---} \overset{\curvearrowleft}{X} \longrightarrow RZ + X$. Once the mechanistic critical point has been reached, however, the reaction, now proceeding by the S_N1 mechanism, will be unconditionally facilitated by increasing electron release, and a relatively large effect is likely to be observed.

Some justification for the above predictions was found in studies of the elimination of alcohols from quaternary ammonium hydroxides¹¹ ($Z = OH^-$; $X = N^+Alk_3$), and an examination of the corresponding hydrolysis of trialkylsulphonium hydroxides and salts ($Z = OH^-$, Br^- , etc.; $X = S^+Alk_3$) gave evidence of a more definite character.¹² The decomposition of trimethylsulphonium hydroxide,

¹¹ E. D. Hughes and C. K. Ingold, *J.*, 1933, 69; E. D. Hughes, C. K. Ingold, and C. S. Patel, *ibid.*, p. 526.

¹² E. D. Hughes and C. K. Ingold, *J.*, 1933, 1571; J. L. Gleave, E. D. Hughes, and C. K. Ingold, *J.*, 1935, 236.

$\text{OH}^- + \text{CH}_3\cdot\text{SMe}_2^+ = \text{CH}_3\cdot\text{OH} + \text{SMe}_2$, and that of the corresponding triethyl compound, both in water at 100° , proved to be of the first order with respect to *each* of the ions concerned; both reactions were bimolecular, the former being the more rapid. Methyl-diisopropyl- and dimethyl-*tert.*-butyl-sulphonium hydroxides decomposed to yield *isopropyl* and *tert.*-butyl alcohol respectively, and both reactions were kinetically of the *first* order; moreover, even considerable additions of extraneous hydroxide ions had no effect in the case of the *tert.*-butyl compound, and the complete replacement of hydroxyl by other ions (*i.e.*, the use of sulphonium salts instead of the hydroxide) was without influence. The latter reaction (elimination of *tert.*-butyl alcohol) was much more rapid than the former; actually the ratio of the velocity coefficients $\text{Bu}^\gamma/\text{Pr}^\beta$ was about 2600, whereas the ratio Me/Et was about 9. The anticipated relationships were thus realised, since the four groups Me, Et, Pr^β and Bu^γ stand in ascending order of electron repulsion ($+I$), and the mechanistic critical point (for dilute aqueous solutions at 100°) was located at some point between ethyl and *isopropyl*. Confirmatory evidence was found in a study of the effects of different anions upon the decomposition of the trimethyl-sulphonium cation. Five anions were employed; in order of descending basicity they were OH' , OPh' , CO_3'' , Br' (Cl'). In ethyl-alcoholic solution the decomposition of the phenoxide, like that of the hydroxide, was of the first order with respect to *each* ion (*i.e.*, kinetically bimolecular), and the carbonate, bromide and chloride decomposed by a unimolecular change, the speed not being influenced by extraneous anions. For the first two anions the velocities varied in the order $\text{OH}' > \text{OPh}'$, whereas the decompositions of the carbonate, bromide and chloride gave speeds which were equal within the limits of experimental precision. It is clear that, while the speed of the bimolecular change will depend upon the basicity of the reagent anion, changes in the latter will not affect the rate of the unimolecular mechanism, since the reagent is here excluded from the measurable stage. The anticipated effects of changes in the anion were thus observed.

An examination of the kinetics of the hydrolysis of a series of alkyl halides has also led to results which are in harmony with the theory of Hughes and Ingold. The alkaline hydrolysis of methyl and ethyl halides in alcohol or aqueous alcohol is bimolecular, the ethyl compound reacting the more slowly (by a factor of about 1/10).¹³ E. D. Hughes, C. K. Ingold, and U. G. Shapiro's investigation of the hydrolysis of *isopropyl* halides in aqueous alcohol has

¹³ C. A. L. de Bruyn and A. Steger, *Rec. Trav. chim.*, 1899, **18**, 41, 311; G. H. Grant and C. N. Hinshelwood, *J.*, 1933, 258.

shown that the bimolecular and the unimolecular reactions proceed here at comparable speeds; the former was slower (about $1/25$) than the corresponding reaction of the ethyl halides (in this case moderate concentrations of alkali lead also to the elimination of propylene, and by suitable adjustment of the conditions and determination of the propylene the individual velocity coefficients for the three reactions were determined).¹⁴ The hydrolysis of *tert.*-butyl halides (in aqueous alcohol or aqueous acetone) was found to be unimolecular, and addition of alkali had no influence; ¹⁵ the speed was greater than that for the *isopropyl* halides under comparable conditions by a factor of about 10^4 . Further, a notable increase in the speed of hydrolysis of *tert.*-butyl halides was caused by increase of the water content of the solvent, as would be expected on the view that the velocity is governed by the ionisation of the halide. Clearly, a change of solvent is likely to cause a movement of the mechanistic critical point, and in the case of a suitable compound might actually lead to a change in the order of the reaction.

Increase in the length of a *n*-alkyl group beyond two carbon atoms does not bring about any large increase in the inductive effect, and it is therefore to be expected that other primary, secondary and tertiary groups will give reaction mechanisms of the same type as those established for ethyl, *isopropyl* and *tert.*-butyl respectively; this has been verified in the hydrolysis of β -*n*-hexyl bromide,¹⁶ β -*n*-octyl bromide¹⁷ (both similar to *isopropyl* halides), and the *tert.*-amyl halides¹⁸ (similar to *tert.*-butyl halides).

Relationships of the same type as those observed among the primary, secondary and tertiary aliphatic halides are found in the araliphyl series CH_3 , CH_2Ph , CHPh_2 , CPh_3 . The kinetics of the alkaline hydrolysis of benzyl chloride are of no simple type¹⁹ and indicate simultaneous bimolecular and unimolecular reactions; benzhydryl chloride in aqueous alcohol gives a first-order reaction independent of added hydroxyl ions,²⁰ and the same applies to α -phenylethyl chloride.²¹ The ease of ionisation of triphenylmethyl halides is well known. It is clear that the hydrolysis of benzyl chloride stands on the border line between the unimolecular and the bimolecular mechanisms, and this explains the fact that alkaline hydrolysis (where $\text{S}_{\text{N}}2$ is favoured by a relatively high concentration of OH') is

¹⁴ J., 1936, 225; E. D. Hughes and U. G. Shapiro, J., 1937, 1177.

¹⁵ E. D. Hughes, J., 1935, 255; K. A. Cooper and E. D. Hughes, J., 1937, 1183.

¹⁶ S. C. J. Olivier, *Rec. Trav. chim.*, 1937, **56**, 247.

¹⁷ E. D. Hughes and U. G. Shapiro, J., 1937, 1192.

¹⁸ E. D. Hughes and B. J. MacNulty, *ibid.*, p. 1283.

¹⁹ S. C. J. Olivier and A. P. Weber, *Rec. Trav. chim.*, 1934, **53**, 869.

²⁰ A. M. Ward, J., 1927, 2285.

²¹ *Idem, ibid.*, p. 445.

accelerated by electron-attractive substituents in the nucleus, whereas in absence of alkali (where conditions are not favourable to S_N2) these substituents cause a decrease of speed. Benzylidene chloride and benzotrichloride have both been shown to undergo unimolecular hydrolysis.¹⁹ In the degradation of a series of aralphenyl-trimethylammonium hydroxides ($R \cdot NMe_3 \cdot OH$, where $R = CH_3$, CH_2Ph , $CHPh_2$) in aqueous solution a change from S_N2 to S_N1 is observed at $R = CHPh_2$.²²

All the above "hydrolytic" reactions, when they occur in aqueous-alcoholic solution, are actually combined hydrolyses and alcoholyses. The reagent YZ is here both water and the alcohol (*i.e.*, $Z = OH$ and OR).

A notable observation has been made by E. D. Hughes, C. K. Ingold, and A. D. Scott²³ in connection with the alcoholysis of α -phenylethyl chloride. Using sodium methoxide ($3.5N$) in anhydrous methyl alcohol or sodium ethoxide ($2.8N$) in anhydrous ethyl alcohol at 70° , they find that the bimolecular reaction is of major importance (in contrast with the unimolecular change in aqueous alcohol referred to above); in the former case 61% and in the latter 92.5% of the total alcoholysis proceeds by the bimolecular mechanism under these conditions. The smaller ionising power of the medium (as compared with aqueous alcohol) depresses reactivity by the S_N1 mechanism, and the greater reactivity of the alkoxide ion (as compared with hydroxyl) favours the S_N2 mechanism.

Hughes and Ingold's theory of aliphatic substitution has been challenged by W. Taylor. In a study of the reactions (hydrolysis + alcoholysis) of methyl, ethyl and *tert.*-butyl bromides in 60% and 80% alcohol in absence of added hydroxide, he found these to be kinetically of the first order, the velocities giving the sequence $Bu^\gamma \gg Me > Pr^\beta > Et$ ²⁴ (the value for Pr^β was taken from the results of Hughes, Ingold, and Shapiro). This sequence was regarded as evidence against the theory of Hughes and Ingold, which predicts for reactions by the unimolecular mechanism (if they could all be realised) $Bu^\gamma > Pr^\beta > Et > Me$. Since, however, a bimolecular reaction inevitably becomes pseudounimolecular if one reagent is present in large excess, the results provide no test of mechanism, as was pointed out by L. C. Bateman and E. D. Hughes;²⁵ on the other hand, the relative speeds $Me > Et$ (for the bimolecular mechanism) and $Bu^\gamma \gg Pr^\beta$ (for the unimolecular mechanism) are to be anticipated on Hughes and Ingold's theory. In a subsequent examination of the hydrolysis of the halides in acetone containing 5% or 10% of water (again water in excess; the ratio of the initial

²² F. D. Hughes and C. K. Ingold, *J.*, 1933, 69.

²³ *J.*, 1937, 1201.

²⁴ *Ibid.*, p. 992.

²⁵ *Ibid.*, p. 1187.

concentrations $[H_2O]/[RBr]$ in the experiments recorded varied from 25 to 70), the same sequence of velocities was obtained.²⁶ Taylor has also measured²⁷ the speed of hydrolysis of *tert.*-butyl bromide and of benzhydryl chloride in acetone containing quantities of water up to 10% (initial ratio $[H_2O]/[RBr]$ from 3.4 to 47). In the case of *tert.*-butyl bromide he emphasises the proportionality between velocity and water concentration for the hydrolysis by 1% and 2% of water; he does not observe such proportionality in the case of benzhydryl chloride, however. On the grounds outlined above, together with certain calculations of the equilibrium concentrations for *tert.*-butyl chloride and benzhydryl chloride²⁷ and a further observation to which reference is made below, Taylor concludes that, contrary to the view of Hughes and Ingold, the hydrolysis of an alkyl halide always proceeds by a bimolecular mechanism in which water appears as a direct reagent.²⁸

If, as Taylor suggests, the hydrolysis of *tert.*-butyl halides is a bimolecular process, it would still, of course, give first-order kinetics when water is present in excess. Hughes and Ingold have pointed out, however,⁸ that, if the water molecule acts as a reagent, it functions either as an acid or as a base, and then a stronger acid (*e.g.*, H_3O^+) or base (*e.g.*, OH^-) will act more powerfully; if this does not occur, then in the rate-determining stage the water is acting as solvent only. The velocity of hydrolysis of *tert.*-butyl chloride was shown to be unaffected by acids or bases, and it was largely on this fact that their views of the reaction mechanism were first based. L. C. Bateman and E. D. Hughes have more recently treated *tert.*-butyl chloride with small quantities of water in formic acid medium;²⁵ the ionising power of this solvent is so high that it is not likely to be changed perceptibly by the addition of small proportions of water. They find that the velocity in the initial stages (*i.e.*, previous to interference by the reversed reaction) is independent of the concentration of water, and, for the whole reaction, constant values of the velocity coefficient were obtained by use of the appropriate expression for a first-order reaction with second-order reversal. They isolated *tert.*-butyl alcohol, but no *tert.*-butyl formate, as the product of the reaction in moist formic acid. Taylor finds²⁹ that *tert.*-butyl chloride is esterified by a mixture of formic acid and calcium formate, and suggests that the first-order reaction observed by Bateman and Hughes was a pseudounimolecular esterification. In a recent publication,³⁰ L. C. Bateman, E. D. Hughes, and C. K.

²⁶ *J.*, 1938, 840.

²⁷ *J.*, 1937, 1853; *J. Amer. Chem. Soc.*, 1938, **60**, 2094.

²⁸ *J.*, 1937, 1962.

²⁹ *Ibid.*, p. 1852.

³⁰ *J. Amer. Chem. Soc.*, 1938, **60**, 3080.

Ingold report that the introduction of *chloroacetate* ions into a solution of *tert.*-butyl chloride in moist formic acid leads to the production of *tert.*-butyl *chloroacetate*, the measured reaction velocity not being increased; it appears, therefore, that Taylor's result was probably due solely to the formate ions which he introduced.

L. P. Hammett and his co-workers,³¹ like Hughes and Ingold, recognise that in the hydrolysis and alcoholysis of alkyl halides there are two competing reaction paths which differ in mechanism and in their dependence upon the structure of the halide. They find that the presence of small quantities of water brings about a large increase in the speed of alcoholysis of benzhydryl chloride,³² and examination of the reaction products has shown that this larger velocity is not due to an independent hydrolysis of the halide, but to a speeding-up of the alcoholysis. They describe the change as "polymolecular," and envisage the formation of a solvation complex of alkyl halide with solvent, within which the rearrangements necessary for reaction occur; they further suggest that the substitution of a water molecule for one of alcohol in this complex might then increase the speed on account of a greater affinity of halide ions for water than for alcohol. C. K. Ingold³³ notes the contrast between this large increase of velocity when small proportions of water are added to alcoholic solutions of benzhydryl chloride and the complete lack of any such catalytic influence by similar small quantities of water upon the speed of hydrolysis of *tert.*-butyl chloride in formic acid (where a constant value of the unimolecular velocity coefficient is found).²⁵ He suggests that, since water is a much better ionising solvent than ethyl alcohol, small quantities will greatly increase the rate of ionisation of the alkyl halide, whereas, since formic acid, like water, is a strongly ionising solvent, no such effect would there be expected.

The reaction undergone by *tert.*-butyl chloride in aqueous alcoholic solution is a simultaneous hydrolysis and alcoholysis, giving a mixture of *tert.*-butyl alcohol and *tert.*-butyl ethyl ether, and A. R. Olson and R. S. Halford³⁴ have given a quasi-thermodynamic treatment of reaction rates in such binary solvent mixtures. Using an expression involving the specific velocities for pure alcohol and pure water, and the partial vapour pressures of these constituents and of the *tert.*-butyl halide, and supposing that the solvent takes part in the reaction, they calculate the rates at intermediate solvent

³¹ J. Steigman and L. P. Hammett, *J. Amer. Chem. Soc.*, 1937, **59**, 2536; N. T. Farinacci and L. P. Hammett, *ibid.*, p. 2542.

³² Compare J. F. Norris and A. A. Morton, *ibid.*, 1928, **50**, 1795.

³³ *Trans. Faraday Soc.*, 1938, **34**, 221.

³⁴ *J. Amer. Chem. Soc.*, 1937, **59**, 2644.

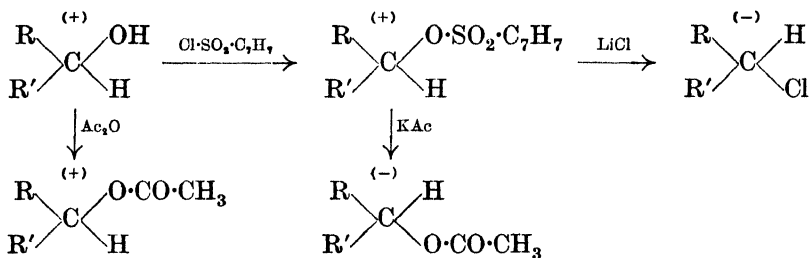
compositions from those observed at two extremes, and also determine the anticipated composition of the reaction product corresponding to each solvent mixture. The calculated *rates* are in agreement with experimental values, and Olson and Halford therefore assume the reaction to be bimolecular. They did not ascertain whether their calculated compositions of the product also agreed with experiment, however. L. C. Bateman, E. D. Hughes, and C. K. Ingold³⁵ have pointed out that, since the solvent doubtless enters into the transition state for *any* reaction in solution (the important rôle of the solvent is emphasised in all the theories to which reference has been made above), Olson and Halford's expression applies equally well to the measurable stage of the unimolecular mechanism. They show further that, since the products of a bimolecular mechanism are formed in the rate-measured stage, whereas those of a unimolecular mechanism are not (for they are formed in subsequent rapid reactions the velocities of which cannot be found), the real test is to determine whether the calculated composition of the product agrees with experiment; only if such agreement is obtained can it be concluded that the products are formed in the rate-measured stage and hence that the reaction is bimolecular. They have determined the proportions of alcohol and ether in the product of the combined hydrolysis and alcoholysis of *tert.*-butyl chloride in three mixtures of water and methyl alcohol and three of water and ethyl alcohol, and find that the proportion of ether is always two to three times larger than that calculated by Olson and Halford. The differences are much greater than the errors in experiment or calculation, and thus a further test has shown the reaction to be unimolecular. Recent work on the Walden inversion has provided yet another method of distinguishing between the bimolecular and the unimolecular mechanisms; this is dealt with below.

The Walden Inversion.—The inversion of configuration which frequently accompanies the replacement of a group linked to a saturated carbon atom, discovered by Walden over forty years ago, has been exemplified by numerous instances where *either* an optically active compound is converted into its stereoisomeride by two replacements *or* the same replacement leads to stereoisomeric products when the reagent or the conditions are varied. The difficulties encountered in detecting the actual change in which inversion takes place and in elucidating the conditions which determine its occurrence have been due partly to the absence of reliable methods of relating sign of rotation to configuration, but also to a lack of knowledge of the mechanism of substitution at a saturated carbon atom. A

³⁵ *J.*, 1938, 881.

notable advance towards the solution of the problem has been made recently. Aided by methods, devised by Kenyon and others, for determining the relative stereochemical configurations of allied compounds, Ingold, Hughes, and their co-workers have been able to carry their researches on aliphatic substitution (see preceding section) into this field, and to link the steric course of a reaction with its mechanism and hence with the factors by which mechanism is determined, *viz.*, the structure of the reacting compound and the conditions under which the replacement occurs.

A list of relative configurations was drawn up twenty-five years ago by P. F. Frankland,³⁶ on the basis of a statistical survey of the recorded effects of different reagents upon replacements at an asymmetric carbon atom, and the recent researches have largely confirmed the conclusions there reached. The assumption made by G. W. Clough,³⁷ *viz.*, that similarity of configuration is accompanied by similarity in the effects of structural and external conditions, appears to have yielded less satisfactory results, although it may be used within prescribed limits.³⁸ A number of theoretical methods by which attempts have been made to relate structure to rotation are summarised by E. D. Hughes.³⁹ J. Kenyon and H. Phillips have used a chemical method which has enabled them to establish configurations with a good degree of certainty. The following scheme is typical of the numerous series of transformations which they have carried out during the past few years :



The (+) and (−) symbols indicate the observed signs of rotation. Of these replacements, it may be assumed that only the reactions of the *p*-toluenesulphonate with acetate or chloride ions involve the rupture of one of the linkages of the asymmetric carbon atom, and therefore an inversion is possible only in these two stages. Since the acetate obtained by direct acetylation of the secondary alcohol, a reaction presumably not involving the asymmetric carbon atom,

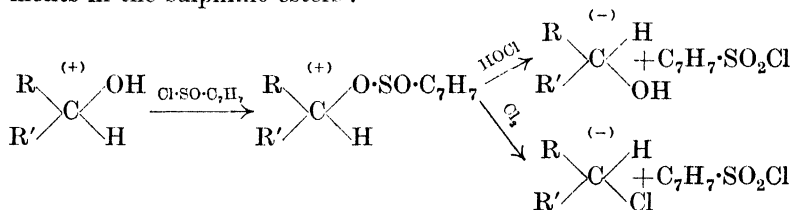
³⁶ *J.*, 1913, **103**, 713.

³⁷ *J.*, 1918, **113**, 526.

³⁸ K. Freudenberg and A. Lux, *Ber.*, 1928, **61**, 1083; *Ann. Reports*, 1929, **26**, 86.

³⁹ *Trans. Faraday Soc.*, 1938, **34**, 202.

has the same sign of rotation as the alcohol, whereas that prepared by the reaction of acetate ion with the *p*-toluenesulphonate has the opposite sign, it may be concluded that inversion occurs in the latter replacement, and hence that the alcohol and the acetate having the same sign of rotation are alike in configuration. By analogy this will apply also to the chloride, but this view demands the assumption that chloride and acetate ions have similar steric effects. The same conclusion regarding the configuration of the chloride is drawn (by making a very similar assumption) from observations of replacements in the sulphinic esters :



On the basis of a procedure of the type outlined above, Kenyon, Phillips, and their co-workers have assigned configurations to derivatives of α -benzylethyl alcohol,⁴⁰ β -*n*-octyl alcohol,⁴¹ ethyl lactate,⁴² α -phenylethyl alcohol,⁴³ and ethyl β -hydroxy- β -phenylpropionate.⁴⁴ The replacement of the sulphonate or sulphinat group (*e.g.*, by OAc, OH) led to inversion in all cases where the configuration of the product was known, and there was thus considerable justification for the assumption that its replacement by chlorine would have the same effect. Moreover, this is in harmony with recent views regarding the Walden inversion,⁴⁵ and its correctness is rendered the more probable since, in the case of β -*n*-octyl iodide,⁴⁶ and also of α -phenylethyl bromide⁴⁷ and of α -bromopropionic acid,⁴⁸ the replacement of a halide ion by one of the same kind (I by I, or Br by Br) has been shown to occur at a rate which is

⁴⁰ H. Phillips, *J.*, 1923, **123**, 44.

⁴¹ *Idem*, *J.*, 1925, **127**, 2564; A. J. H. Houssa, J. Kenyon, and H. Phillips, *J.*, 1929, 1700; *Ann. Reports*, 1929, **26**, 87.

⁴² J. Kenyon, H. Phillips, and H. G. Turley, *J.*, 1925, **127**, 399; *Ann. Reports*, 1926, **23**, 110.

⁴³ J. Kenyon, H. Phillips, and F. M. H. Taylor, *J.*, 1933, 173.

⁴⁴ J. Kenyon, H. Phillips, and G. R. Shutt, *J.*, 1935, 1663; *Ann. Reports* 1935, **32**, 244.

⁴⁵ Refs. 54, 55, 56.

⁴⁶ E. D. Hughes, F. Juliusburger, S. Masterman, B. Topley, and J. Weiss, *J.*, 1935, 1525.

⁴⁷ E. D. Hughes, F. Juliusburger, A. D. Scott, B. Topley, and J. Weiss, *J.*, 1936, 1173.

⁴⁸ W. A. Cowdrey, E. D. Hughes, T. P. Nevell, and C. L. Wilson, *J.*, 1938, 209.

quantitatively equivalent to the speed of racemisation. In the work here referred to, the organic halide in acetone solution was treated with sodium iodide (or lithium bromide) containing the radioactive isotope of the halogen, and the rate of exchange of halogen (*e.g.*, $\text{RI} + \text{NaI}^* = \text{RI}^* + \text{NaI}$, where I^* represents the radioactive isotope) was determined by measurement of the intensities of radioactivity of the alkyl halide or the alkali halide after known time intervals. The velocity of racemisation was found polarimetrically, and in all three instances the rates of exchange and racemisation were equivalent within experimental error. There seems to be little doubt, therefore, that inversion occurs when a halide ion replaces another anion, and that the configurations arrived at by Kenyon and Phillips are correct. A knowledge of these configurations was essential in the recent work now to be described.

The earlier theories of the Walden inversion⁴⁹ postulated the initial formation of an addition product, and the opposite view, that of an ionisation process as the first step, has been considered by T. M. Lowry⁵⁰ and by J. Kenyon and H. Phillips.⁵¹ The remaining alternative,⁵² *viz.*, that substitution involves a simultaneous addition of one group and removal of the other, as was suggested in connection with the Walden inversion by G. N. Lewis,⁵³ has appeared in recent theories due to A. R. Olson⁵⁴ and N. Meer and M. Polanyi.⁵⁵ Olson postulates inversion in every substitution, and Meer and Polanyi predict inversion for certain types of substitution. When an anionic group X (*e.g.*, OH, Cl) is linked to the asymmetric carbon atom, the dipole associated with the bond has the direction $\overset{+}{\text{C}}-\bar{\text{X}}$, and an

⁴⁹ Summarised in *Ann. Reports*, 1911, **8**, 60; also P. F. Frankland, ref. 36. A. Meisenheimer (*Annalen*, 1927, **456**, 126) has more recently put forward a development of views of this type.

⁵⁰ Deuxième Conseil de Chimie Solvay, 1925, p. 39.

⁵¹ *Trans. Faraday Soc.*, 1930, **26**, 451.

⁵² A comprehensive survey of theories of the Walden inversion would also include reference to the postulates of B. Holmberg (*Ber.*, 1926, **59**, 125) and H. N. K. Rørdam (*J.*, 1928, 2447; 1929, 1282; 1930, 2017). The former bases his argument upon the relative distances $\text{C} \longleftrightarrow \text{X}$ and $\text{B} \longleftrightarrow \text{Y}$ ("reaction distances") in the compound R_3CX and the reagent BY , but it is difficult to understand the meaning of the term when the reagent is an anion; he considers, however, that inversion will be the general rule in this case, as is indicated by his experimental results. Rørdam distinguishes between replacements brought about by an anion and those brought about by a molecule (*e.g.*, PCl_5) which itself removes the replaced group. He supposes that the position taken up by the entering group will depend upon the phase of oscillation of the three radicals still linked to the asymmetric carbon atom at the moment of entry.

⁵³ "Valence and the Structure of Atoms and Molecules." 1923, p. 113.

⁵⁴ *J. Chem. Physics*, 1933, **1**, 418.

⁵⁵ *Z. physikal. Chem.*, 1932, **B**, **19**, 164.

approaching negative ion, under the influence of the electrostatic forces, therefore attacks the carbon atom on the side away from the group X; "the group which is to be displaced determines a unique path for the entering group such that the system requires less energy than it would for any other path."⁵⁴ The conclusion is thus reached that inversion always occurs in the bimolecular replacement of an anionic group by a negative ion,⁵⁶ and in addition to the evidence provided by Olson and Polanyi themselves, relating mainly to reactions between halide ions and alkyl halides or halogeno-acids,⁵⁷ this view is supported by the results, already referred to, of investigations by Kenyon and Phillips and by E. D. Hughes and his co-workers.^{46, 47, 48} Meer and Polanyi distinguish between these replacements by an anion ("negative mechanism") and those in which the attack is by a cation ("positive mechanism"); they consider that the latter would not in general lead to inversion, although doubt is expressed regarding certain instances.⁵⁸

In a detailed discussion of the problems presented by the steric course of substitution, W. A. Cowdrey, E. D. Hughes, C. K. Ingold, S. Masterman, and A. D. Scott⁵⁹ employ the theory of simultaneous addition and dissociation in conjunction with that of initial dissociation, and the knowledge of reaction mechanism gained by the kinetic studies to which reference has already been made (preceding section) is applied to the prediction and interpretation of the steric course of the substitution. Their general conclusions are that bimolecular substitutions (S_N2 , S_E2 ; see preceding section) are invariably accompanied by inversion, whereas unimolecular substitution (S_N1 , S_E1) may lead to inversion, retention of configuration, or racemisation, the actual result being dependent upon other circumstances.

Inversion of configuration in a bimolecular substitution is ascribed, not to the direction of the dipole $\overset{+}{C}-\bar{X}$, but to the fact that, on account of forces of shorter range than dipole forces, the most favourable method of attack is along the line of this linking, i.e., $Y \cdots \cdots \nearrow C-X$.⁹ Such a view is confirmed by J. Read and J. Walker's observation of inversion in the replacement by OH of NMe_3 in *l*-piperityltrimethylammonium hydroxide;⁶⁰ the bond to

⁵⁶ Compare B. Holmberg, ref. 52; J. Steigman and L. P. Hammett, ref. 31; J. Kenyon and H. Phillips, ref. 51; P. A. Levene, A. Rothen, and M. Kuna, *J. Biol. Chem.*, 1937, **121**, 747. "The molecule is turned inside out like an umbrella in a strong wind" (*Ann. Reports*, 1935, **32**, 95).

⁵⁷ A. R. Olson and F. A. Long, *J. Amer. Chem. Soc.*, 1934, **56**, 1294; A. R. Olson and H. H. Voge, *ibid.*, p. 1690; E. Bergmann, M. Polyani, and A. L. Szabo, *Z. physikal. Chem.*, 1933, **20**, 161; *Trans. Faraday Soc.*, 1936, **32**, 843.

⁵⁸ M. Polanyi, "Atomic Reactions," 1932, p. 63.

⁵⁹ *J.*, 1937, 1252.

⁶⁰ *J.*, 1934, 308.

be ruptured is $\text{C}-\text{NR}_3^+$, and the electrostatic forces would here direct the attacking anion to a position giving a retained configuration, whereas the experimental results indicate that the attack is on the opposite side. The configuration of the product of a unimolecular substitution, in which the first step is the formation of a carbon anion or cation, is determined, according to Ingold and his co-workers, by the life of the ion. The available examples relate to nucleophilic substitutions ($\text{S}_{\text{N}}1$), where the positive ion is flat. If this ion has a relatively long life (as will be the case if the reactivity of the ion itself or of the medium is low, or if the dilution of the reagent is high), substitution at either side will occur with equal facility, giving a racemic product. A cation of short life, however, will be shielded by the receding anion during the period in which the position of substitution is determined, and substitutions with inversion will outnumber those in which the configuration is retained; the net result is a predominating inversion, but with more or less racemisation. In special instances, however (see later), there may be considerable retention of configuration. These predictions have been tested by a kinetic and polarimetric study of the hydrolysis and alcoholysis of β -*n*-octyl halides, α -phenylethyl halides and α -bromopropionic acid, its anion, and its ester.

Of these examples, the simplest is that of the β -*n*-octyl halides, where only neutral, saturated substituents are present at the seat of substitution. E. D. Hughes and U. G. Shapiro¹⁷ have shown that in general (as is the case with other secondary halides; see preceding section) the substitution occurs by both the bimolecular and the unimolecular mechanisms ($\text{S}_{\text{N}}2$ and $\text{S}_{\text{N}}1$), but suitable conditions cause one or the other mechanism to take almost complete control. E. D. Hughes, C. K. Ingold, and S. Masterman⁶¹ find that the bimolecular hydrolysis or alcoholysis proceeds with inversion of configuration and an almost quantitative preservation of rotatory power, while the unimolecular substitution takes place with predominating inversion but considerable racemisation; this is in complete agreement with the predictions outlined above. The phenyl substituent in α -phenylethyl halides introduces resonance which tends both to stabilise and to flatten the ion. The bimolecular hydrolysis of this halide cannot be realised experimentally,²¹ but E. D. Hughes, C. K. Ingold, and A. D. Scott⁶² have shown that bimolecular alcoholysis leads to inversion with a high retention of rotatory power, while unimolecular hydrolysis and alcoholysis lead to inversion with very extensive racemisation. The aryl group increases both the relative importance of mechanism $\text{S}_{\text{N}}1$ and the extent to which racemisation accompanies substitution by this

⁶¹ *J.*, 1937, 1196.⁶² *Ibid.*, p. 1201.

mechanism. The definite character of the above results and their agreement with theoretical predictions make it justifiable to draw two conclusions,⁵⁹ viz.: (a) in the homogeneous hydrolysis and alcoholysis of alkyl halides, whatever mechanism be involved, inversion predominates, and this rule may be employed in relating configuration to sign of rotation; (b) extensive racemisation always accompanies the unimolecular mechanism and is absent in the bimolecular mechanism; this provides an additional method of determining mechanism.

The groups —CO·OH and —CO·OR are strongly electron-attractive; their attachment at the seat of substitution therefore favours reaction by the bimolecular mechanism, and W. A. Cowdrey, E. D. Hughes, and C. K. Ingold⁶³ find that the hydrolysis and alcoholysis of α -bromopropionic acid and its methyl ester occur with inversion and no appreciable racemisation. The presence of the negatively charged carboxylate group (an electron-repelling group) in the α -bromopropionate anion, on the other hand, favours mechanism $\text{S}_{\text{N}}1$; it also tends to stabilise the ion and to preserve a pyra-

midal configuration, since the ion is a betaine $\begin{array}{c} \text{CO} \\ \diagup \quad \diagdown \\ -\text{O} \quad \text{C}^+ \end{array}$; this

structure is likely to remain until a new group enters the position vacated by the one expelled, and the result will be a considerable retention of configuration. An investigation of the hydrolysis and alcoholysis of sodium α -bromopropionate by Cowdrey, Hughes, and Ingold⁶³ has demonstrated the occurrence of reaction by both mechanisms; mechanism $\text{S}_{\text{N}}2$ proceeds, as usual, with inversion, while $\text{S}_{\text{N}}1$ gives an almost complete retention of the original configuration. The above results have been tabulated very clearly by E. D. Hughes.³⁹

The reactions of alkyl halides with silver oxide or with soluble silver salts (*e.g.*, $\text{RCl} + \text{AgNO}_3 + \text{H}_2\text{O} = \text{ROH} + \text{AgCl} + \text{HNO}_3$) involve a heterogeneous attack by silver ions upon the halide adsorbed on the surface of solid silver oxide or halide.^{64, 65, 66} It may be supposed⁵⁹ that the C-halogen bond of the adsorbed halide is stretched and thereby weakened, this making it possible for an adsorbed silver ion to remove the halogen; finally, reaction occurs between the ion and an adsorbed reagent or solvent molecule. This view, which postulates a heterogeneous ionisation, leads to the expectation of a similarity between these processes and homogeneous unimolecular hydrolysis ($\text{S}_{\text{N}}1$), and the results of Ingold, Hughes, and

⁶³ *J.*, 1937, 1208.

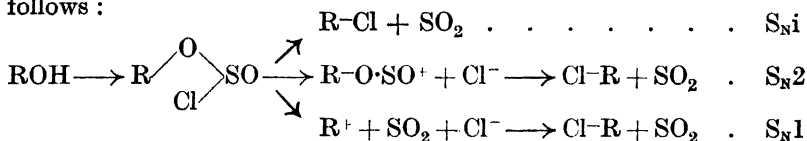
⁶⁴ G. Senter, *J.*, 1910, **97**, 346; 1911, **99**, 95.

⁶⁵ E. D. Hughes, C. K. Ingold, and S. Masterman, *J.*, 1937, 1236.

⁶⁶ W. A. Cowdrey, E. D. Hughes, and C. K. Ingold, *ibid.*, p. 1243.

their co-workers have shown that such a similarity actually exists. The hydrolysis and alcoholysis of β -*n*-octyl halides by means of silver oxide, nitrate or acetate in aqueous alcohol gives predominating inversion and some racemisation; α -phenylethyl chloride under similar conditions behaves in the same way, but more extensive racemisation occurs.⁶⁵ The alcoholysis of methyl α -bromopropionate by silver nitrate in methyl alcohol leads to inversion with racemisation, while in presence of either silver oxide or silver nitrate substitution in the α -bromopropionate ion is far more rapid than in the undissociated acid or its ester (even in fairly concentrated solutions of mineral acid the reaction of α -bromopropionic acid with aqueous silver nitrate proceeds almost entirely through the anion),⁶⁷ giving a predominating retention of configuration but some accompanying racemisation.⁶⁶ The anticipated analogy of the heterogeneous reaction with unimolecular homogeneous substitution is thus realised.

In their discussion of these problems, Ingold and his collaborators⁵⁹ have applied their views to numerous observations from the literature, and have also constructed tables showing relationships between molecular configuration and the sign of optical rotation in a number of compounds; in general their configurations are in agreement with those of Frankland.³⁶ Recorded data for the replacement of hydroxyl by halogen through the agency of phosphorus or sulphur halides or of halogen acids are also considered. The facts relating to these substitutions indicate that inversion is the general rule;⁶⁸ in substitutions by thionyl chloride, however, inversion is not observed if a phenyl group is attached to the asymmetric carbon atom, although this peculiarity disappears if a tertiary amine is present.⁶⁹ The reactions with hydrogen halides appear to give racemisation in addition. The mechanisms put forward by Ingold and his collaborators to represent these changes are all of the same type, and may be illustrated by reference to the replacement of hydroxyl by chlorine through the agency of thionyl chloride. The first step postulated is the formation of a compound $R\cdot O\cdot SOCl$, which can then undergo three distinct changes, as follows :



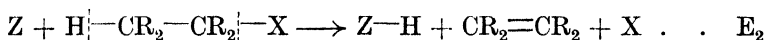
⁶⁷ A suppression of ionisation by the nitric acid liberated in the reaction accounts for a downward drift in the second-order velocity coefficients for the hydroxylation of α -halogenated acids by aqueous silver nitrate (G. Senter, ref. 64; H. Euler, *Ber.*, 1906, **39**, 2726).

⁶⁸ Compare P. F. Frankland, ref. 36.

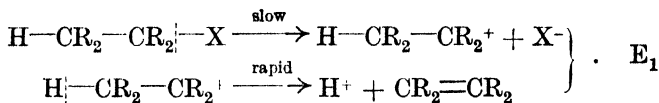
⁶⁹ J. Kenyon, A. G. Lipscomb, and H. Phillips, *J.*, 1930, 415.

The first change (S_N1) is a "rearrangement" (actually a nucleophilic substitution in which two bonds are ruptured) which results in a retention of the original configuration; S_N2 and S_N1 are respectively bimolecular and unimolecular substitutions in the cation of $R\cdot O\cdot SOCl$, and lead to inversion (S_N2) and inversion with racemisation (S_N1) in accordance with the principles already established. A phenyl substituent at the point of substitution will promote reaction by S_N1 (configuration retained) owing to its capacity for electromeric electron-release, but a tertiary base will favour the ionisation mechanisms which lead to inversion owing to the production of its hydrochloride. The application to other recorded observations may be found in the original paper, together with lists of compounds having corresponding configurations.

Elimination Reactions.—Olefin elimination frequently occurs side by side with substitution in saturated compounds (*e.g.*, alkyl halides, quaternary ammonium hydroxides, etc.), and the demonstration of a dual mechanism for the latter suggests a similar possibility for the former. The mechanism of elimination reactions put forward by W. Hanhart and C. K. Ingold ⁷⁰ may be written



In this bimolecular reaction, a basic reagent Z extracts a proton simultaneously with the separation of an anionic group X; the hydrogen and the anionic group must be linked to adjacent carbon atoms in order that octets may be preserved. Since the formulation of this mechanism, studies of olefin elimination have been reported in various papers by C. K. Ingold and his collaborators, and in their most recent contribution to the subject they bring forward evidence of a unimolecular mechanism,* *viz.*,

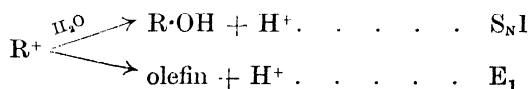


In a search for reactions proceeding by the unimolecular mechanism, the non-basic but strongly ionising solvents sulphur dioxide and formic acid were used; these media can ionise alkyl halides but cannot bring about substitution or bimolecular (pseudounimolecular) elimination (as, *e.g.*, in $H_2O + NO_2\cdot C_6H_4\cdot CH_2\cdot CH_2\cdot NMe_3 = H_3O^+ + NO_2\cdot C_6H_4\cdot CH\cdot CH_2 + NMe_3$, where water is a sufficiently strong base to remove the proton, and the presence of a stronger base

⁷⁰ J., 1927, 997; *Ann. Reports*, 1930, 27, 143.

* W. Taylor (ref. 28) has proposed a bimolecular mechanism for *all* elimination reactions (as for all substitutions). This does not appear to differ from Ingold's E_2 mechanism.

increases the speed).⁷¹ The halides chosen for the investigation were α -phenylethyl chloride and *tert.*-butyl chloride, both of which undergo substitution by the unimolecular mechanism S_N1 , and also contain a hydrogen in the correct position for the elimination reaction. In both sulphur dioxide and formic acid the halides were shown to come spontaneously into equilibrium with olefin and hydrogen chloride.⁷² The work was extended to aqueous media by a study of the elimination reactions accompanying substitution in β -*n*-octyl, *tert.*-butyl, and *tert.*-amyl halides in aqueous alcohol.⁷³ The speed of the elimination reaction was measured by estimation of the olefin at given time intervals; this was found to give first-order kinetics, but, in view of the basic nature of the medium, the reaction mechanism was not thereby established. The following test was therefore applied. The postulated rate-controlling process for both substitution and elimination is the same, *viz.*, the ionisation of the alkyl halide, $RX \longrightarrow R^+ + X^-$, and the subsequent (rapid) step is a reaction of the organic cation alone :



The *total* velocity (that of the ionisation) will therefore depend upon the nature both of the alkyl group R and of the halogen, but the *relative* speeds of substitution and elimination (which govern the proportion of olefin in the product) are independent of the halogen and depend only upon the group R. For two halides having the same alkyl group (*e.g.*, β -*n*-octyl chloride and bromide), therefore, the ratios of the velocity of elimination (k_E) to the total velocity (k_1) should not be very different. Absolute equality of these ratios cannot be expected, since other factors intervene (*e.g.*, the shielding of the cation by the departing anion).⁷⁴ Nevertheless, the proportion of the total first-order reaction which results in elimination (k_E/k_1) should depend essentially upon R, and be modified to a relatively small degree by changes in the halogen. The experimental results are summarised below :

R.		Ratio of k_1 values RCl/RBr.	Ratio k_E/k_1 for RCl.	Ratio k_E/k_1 for RBr.
β - <i>n</i> -Octyl	(100° in 60% alcohol)	33	0.13	0.14
<i>tert.</i> -Butyl	} (25° in 80% alcohol) {	44	0.17	0.13
<i>tert.</i> -Amyl		39	0.33	0.26

⁷¹ E. D. Hughes and C. K. Ingold, *J.*, 1933, 523.

⁷² E. D. Hughes, C. K. Ingold, and A. D. Scott, *J.*, 1937, 1271.

⁷³ E. D. Hughes, C. K. Ingold, and U. G. Shapiro, *ibid.*, p. 1277; K. A. Cooper, E. D. Hughes, and C. K. Ingold, *ibid.*, p. 1280; E. D. Hughes and B. J. MacNulty, *ibid.*, p. 1283.

⁷⁴ Compare this report, p. 223.

The significant feature is the contrast between the *large* differences in velocity and the accompanying *small* differences in the k_x/k_1 ratio when alkyl chlorides are compared with the corresponding bromides. This is in harmony with the predictions of Ingold and Hughes.

Prototropic Changes.—Prototropic systems (*e.g.*, $\text{HX}-\text{Y}=\text{Z} \rightleftharpoons \text{X}=\text{Y}-\text{ZH}$) may be classified as (a) thermodynamically balanced and (b) thermodynamically unbalanced. In those of the former class, both tautomerides are of the same order of stability and the catalysed transformation of the one into the other may be followed by analytical methods. This procedure is not applicable to systems of the second type, however, since the concentration of one form is at no time sufficiently high for measurement. Many keto-enol systems belong to this class, and the velocity of the prototropic change may here be determined by Lapworth's halogenation method. Most carbonyl compounds react instantaneously with halogens subsequently to a catalysed prototropic change which is the rate-determining step; simple monocarboxylic acids and their derivatives are not included in this generalisation, for they give no evidence of prototropy (*e.g.*, the speed of bromination of acetyl bromide is directly proportional to the concentration of the halogen).¹ J. B. Conant and G. H. Carlson² have introduced a third method for the measurement of rates of prototropic changes; this can be employed in cases where the atom from which the mobile proton migrates is a centre of asymmetry, and where the rate of loss of optical activity can therefore be determined (*e.g.*, $\text{R}\cdot\text{CO}\cdot\text{CHR}^1\text{R}^2 \longrightarrow \text{R}\cdot\text{C}(\text{OH})\cdot\text{CR}^1\text{R}^2$). By a combination of the second and the third of the above methods, P. D. Bartlett and his collaborators³ have estimated the relative contributions made by the two groups capable of providing a proton in ketones of the type $>\text{CH}\cdot\text{CO}\cdot\text{CH}<$, where one α -carbon is asymmetric; the halogenation is a measure of the sum of the changes into the isomeric enols, whereas the loss of optical activity is determined by the change into one of these. They have shown, for example, that in the acid-catalysed prototropy of menthone in glacial acetic acid, 79% of the prototropic change involves the hydrogen linked to C_4 . The acid-catalysed racemisation of menthone, phenylmethylacetophenone and phenylisobutylacetophenone in non-hydroxylic solvents has recently been studied by R. P. Bell and his co-workers;⁴ the absence of basic characters in the medium here introduces some special features.

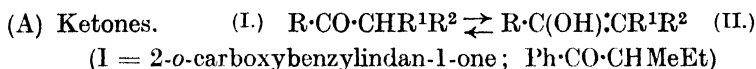
¹ H. B. Watson, *J.*, 1925, **127**, 2067; 1928, 1137; *Chem. Reviews*, 1930, **7**, 173.

² *J. Amer. Chem. Soc.*, 1932, **54**, 4048; *Ann. Reports*, 1934, **31**, 197.

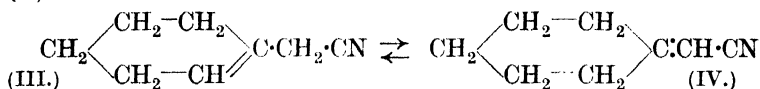
³ P. D. Bartlett and J. R. Vincent, *J. Amer. Chem. Soc.*, 1933, **55**, 4992; P. D. Bartlett and C. H. Stauffer, *ibid.*, 1935, **57**, 2580.

⁴ R. P. Bell and E. F. Caldin, *J.*, 1938, 382; R. P. Bell, O. M. Lidwell, and J. Wright, *ibid.*, p. 1861.

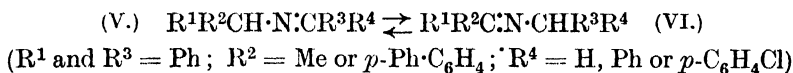
Reference was made two years ago⁵ to the measurements of speeds of prototropic reactions by C. K. Ingold and C. L. Wilson,⁶ who employed all of the above methods. This work has now been extended to include yet a fourth method, *viz.*, the determination of the rate at which hydrogen is exchanged for deuterium.⁷ Three different systems have been investigated :



(B) Unsaturated nitriles.⁸



(C) Methylenazomethines.



In all comparisons the conditions were standardised as completely as possible, and the results may be summarised as follows :

(A) For ketones, the speeds of racemisation, bromination and deuterium exchange, all base-catalysed, are equal within the limits of experimental uncertainty.* The rates of the acid-catalysed racemisation and bromination are also equal (this equality was found for methylethylacetophenone by Bartlett and Stauffer).³

(B) In the case of the unsaturated nitriles, the less stable isomeride (III) exchanges hydrogen for deuterium far more rapidly than it is converted into (IV).

(C) In the methylenazomethine system the speeds of racemisation and interconversion are equal, and this equality has been confirmed by G. T. Borchardt and H. Adkins⁹ for the case where $R^1 = R^3$ = Ph, R^2 = Me, and R^4 = *p*-C₆H₄Cl. The rate of deuterium exchange is much greater, however.

⁵ *Ann. Reports*, 1936, **33**, 232.

⁶ C. K. Ingold and C. L. Wilson, *J.*, 1933, 1493; 1934, 93, 773; C. L. Wilson, *J.*, 1934, 98; S. K. Hsü, C. K. Ingold, and C. L. Wilson, *J.*, 1935, 1778; S. K. Hsü and C. L. Wilson, *J.*, 1936, 623.

⁷ C. K. Ingold, E. de Salas, and C. L. Wilson, *J.*, 1936, 1328; S. K. Hsü, C. K. Ingold, and C. L. Wilson, *J.*, 1938, 78; E. de Salas and C. L. Wilson, *ibid.*, p. 319. Summarised by C. L. Wilson, *Trans. Faraday Soc.*, 1938, **34**, 175.

⁸ See also A. Kandiah and R. P. Linstead, *J.*, 1929, 2139.

⁹ *J. Amer. Chem. Soc.*, 1938, **60**, 3.

* D. J. G. Ives and G. C. Wilks (*J.*, 1938, 1455) have more recently observed equal rates of racemisation and exchange in the phenyl-*p*-tolyldeuteroacetate ion.

Ingold and Wilson interpret their results on the basis of the commonly accepted view that the first step in the base-catalysed change ("basic mechanism") is the transfer of the mobile proton to the catalyst; in catalysis by acids ("acid mechanism") transference of this proton to an acceptor in the medium is made more easy by initial co-ordination of the molecule with the acid. This point of view is essentially that put forward by A. Lapworth and A. C. O. Hann,¹⁰ and it has more recently been expressed fully by K. J. Pedersen,¹¹ who points out that it implies that there is no difference in principle between the acidic characters of a ψ -acid (e.g., ketone, nitro-compound) and of a true acid (e.g., enol, *iso*-nitro-compound), since both are genuine acids although the former is much weaker than the latter.

The equality of the speeds of base-catalysed racemisation, bromination and deuterium exchange for the ketones studied by Ingold and Wilson indicates that all three reactions are controlled by the same fundamental process, which, in accordance with the ionisation theory of prototropy, is believed to be the removal of

the α -proton with formation of the mesomeric anion $\overline{\text{C}-\overset{\ominus}{\text{C}}-\text{O}}$ (a resonance structure between $\bar{\text{C}}-\text{C}=\text{O}$ and $\text{C}=\text{C}-\bar{\text{O}}$). This ion is regarded as the active agent in bromination and deuterium exchange, and the measured (equal) speeds are therefore equated to the speed of ionisation; even if the thermodynamically unstable enol is formed, the union of the ions will be practically instantaneous and the result will be the same. R. H. Kimball¹² has found, however, that the *l*-menthyl ester of *d*- β -keto- α -phenyl-*n*-butyric acid (in *cyclohexane*) loses its optical activity about three times as rapidly as it passes into its enolic form (which here constitutes about 71% of the equilibrium mixture); it appears, therefore, that the asymmetry is lost in the ion, which may subsequently accept a proton *either* to regenerate the ketone *or* to form enol (since both forms are, in this case, of comparable stability, and their rates of production from the mesomeric ion are therefore of the same order). The rate of tautomeric conversion is therefore less than that of ionisation (and hence of racemisation). The difference in the speeds of isomerisation and deuterium exchange for the unsaturated nitrile (III) is interpreted similarly; every anion formed from (III) leads to deuterium exchange with the medium, but not every anion yields (IV), some reverting to (III). An analogous observation has been

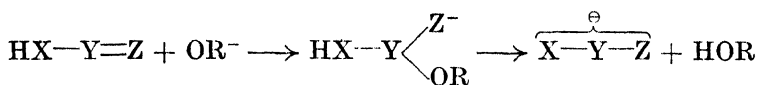
¹⁰ *J.*, 1902, **81**, 1512.

¹¹ *J. Physical Chem.*, 1933, **37**, 751; 1934, **38**, 581, 601; *Trans. Faraday Soc.*, 1938, **34**, 237.

¹² *J. Amer. Chem. Soc.*, 1936, **58**, 1963; *Ann. Reports*, 1936, **33**, 234.

made by D. J. G. Ives¹³ for the three-carbon system in the vinylacetate ion; the speed of the exchange reaction is greater than that of the conversion into crotonate ion. In the methyleneazomethine system, also, the tautomerides are of similar stability, and every ionisation process would be expected to lead to loss of optical activity but not to isomerisation. Here, however, the observed velocities are equal. It is therefore suggested that the anion does not attain kinetic independence, but that the removal of the one proton and the addition of the other occur in one synchronised act; under these conditions racemisation would not be more rapid than isomerisation (the greater rate of deuterium exchange is ascribed to the operation of some additional mechanism). Systems having mobile hydrogen can be arranged in a series of descending acidity; such a series passes from carboxylic acids $\text{HO}-\text{C}=\text{O}$, through ketones $\text{HC}-\text{C}=\text{O}$ and nitro-compounds $\text{HC}-\text{N}=\text{O}$, to unsaturated hydrocarbons $\text{HC}-\text{C}=\text{C}$ and methyleneazomethines $\text{HC}-\text{N}=\text{C}$, and Ingold and Wilson consider that the kinetic independence of the anion shows a steady decrease until in the last member the dissociation and reassociation processes overlap in time and the anion never becomes free.

The ionisation theory of base-catalysed prototropy, in postulating the direct removal of a proton from its combination with carbon, thus implies an analogy of prototropic systems with the more powerfully acidic systems (*e.g.*, carboxylic acids) in which hydrogen linked to oxygen is ionisable. It has been suggested¹⁴ that the primary process may rather be analogous to cyanohydrin formation or the alkaline hydrolysis of esters, in which the base is added at carbonyl carbon. The anion would then be formed in two steps instead of one, as follows :



As might be anticipated, electron-attractive substituents in a ketone molecule facilitate base-catalysed prototropy and operate against the acid-catalysed reaction.* This has been demonstrated, for example, in a series of nuclear-substituted acetophenones.¹⁵ The favourable influence of electron-attractive groups upon base-

¹³ *J.*, 1938, 91.

¹⁴ H. B. Watson, W. S. Nathan, and L. L. Laurie, *J. Chem. Physics*, 1935, 3, 170.

¹⁵ W. S. Nathan and H. B. Watson, *J.*, 1933, 217; D. P. Evans, V. G. Morgan, and H. B. Watson, *J.*, 1935, 1167; V. G. Morgan and H. B. Watson, *ibid.*, p. 1173.

* A similar remark does not apply to acid hydrolysis of esters; see p. 238.

catalsed prototropy has been observed in a number of systems (*e.g.*, three-carbon tautomerism,¹⁶ prototropy of $\alpha\gamma$ -diphenylpropenes and $\alpha\gamma$ -diphenylmethylenazomethines),¹⁷ and quite recently it has been shown that the halogen atom in α -bromo- $\beta\beta$ -diphenylpropionylmesitylene very greatly increases the ease with which the compound is converted into enol.¹⁸ It follows, of course, that in systems where prototropy may occur by either the "acid mechanism" or the "basic mechanism," the presence of electron-attractive groups in the vicinity of the reactive centre will tend to cause the change to follow the latter route. This is found, for example, in the bromination of ethyl acetoacetate and of ethyl pyruvate.¹⁹ A further example has been revealed in a study of the bromination of a series of halogenated acetones in 50% and 75% acetic acid containing hydrogen chloride;²⁰ as the number of halogen atoms in the molecule increases, the isocatalytic point moves steadily to a region of higher acid concentration, until $\alpha\alpha\alpha$ -tribromo- and *as*-tetrabromo-acetones are brominated by the "basic mechanism" even in presence of 2M-hydrogen chloride. In view of this powerful effect of halogen substituents in promoting reaction by the "basic mechanism," it is not surprising that the speed of interaction of acetone with alkaline hypobromite or hypoiodite (haloform reaction) is governed by the rate of prototropic change of the acetone itself, the subsequent stages being relatively instantaneous²¹ (the case of hypochlorite is peculiar and a *slow* reaction of OCl^- ion with the enol is suggested). The susceptibility of the higher halogenated acetones to base-catalysed prototropy is, of course, to be correlated with the stability of their hydrates and other addition compounds. Moreover, an electrometric study of dilute aqueous solutions of a number of halogenated acetones²² has shown that in such solutions the mono- and di-chlorinated ketones exchange chlorine for hydroxyl, hexachloroacetone suffers haloform cleavage, and penta-chloro- and *as*-tetrabromo-acetones undergo both these changes. The accumulation of halogen substituents at the α -position renders the carbonyl group more and more reactive towards nucleophilic reagents, and the CX_3 group (which must stand adjacent to carbonyl to make the haloform cleavage possible)²³ is eliminated

¹⁶ C. K. Ingold, C. W. Shoppee, and J. F. Thorpe, *J.*, 1926, 1477.

¹⁷ C. W. Shoppee, *J.*, 1930, 968; 1931, 1225; 1932, 696.

¹⁸ E. P. Kohler and H. M. Sonnichsen, *J. Amer. Chem. Soc.*, 1938, **60**, 2650.

¹⁹ K. J. Pedersen, *ref.* 11; H. B. Watson and E. D. Yates, *J.*, 1933, 220.

²⁰ H. B. Watson and E. D. Yates, *J.*, 1932, 1207.

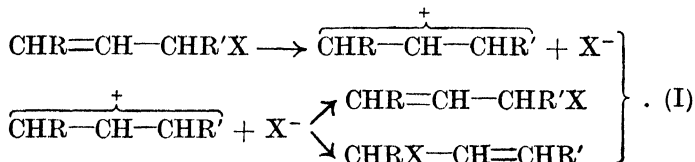
²¹ P. D. Bartlett, *J. Amer. Chem. Soc.*, 1934, **56**, 967.

²² E. G. Edwards, D. P. Evans, and H. B. Watson, *J.*, 1937, 1942.

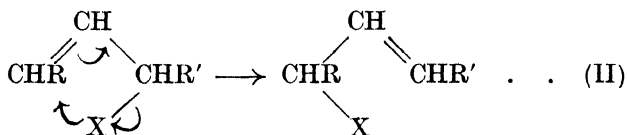
²³ See summary by R. C. Fuson and B. A. Bull, *Chem. Reviews*, 1934, **15**, 275.

in the same manner as the OR group of an ester in alkaline hydrolysis.

Anionotropic Systems.—Some ten years ago, H. Burton and C. K. Ingold brought forward evidence in favour of the view that the interconversion of the tautomerides in an anionotropic system (as in a prototropic system) involves the ionisation of the migrating group : ²⁴



This mechanism was based upon the effects of variations in the nature of the substituent R', of the anionic group X, and of the medium. It was intended to apply primarily to changes in ionising media, and in solvents of poor ionising power or in the absence of a solvent it is quite conceivable, as E. D. Hughes has suggested,²⁵ that the interconversion might occur without separation of X :



The two mechanisms are clearly the analogues of S_N1 and S_N2 for aliphatic substitution.²⁶ Their simultaneous operation may explain the observation, made by J. Kenyon, S. M. Partridge, and H. Phillips,²⁷ that the anionotropic change of an optically active form of CHMe·CH·CHPhX, where X is OH or o-O·CO·C₃H₄·CO₂H, takes place with some racemisation but predominating inversion, as much as 70% of the optical activity being preserved ;²⁸ changes in the medium are here without a marked influence, and the authors suggest a non-ionic mechanism.

Investigations of the replacement of the anionic group X by a different group Y have led to interesting results. It is evident that the group Y may become linked either to the carbon atom from which X is removed (C_a) or to another carbon atom (C_β), and also that the substitution may occur in one synchronous act or by the

²⁴ *Ann. Reports*, 1928, **25**, 127.

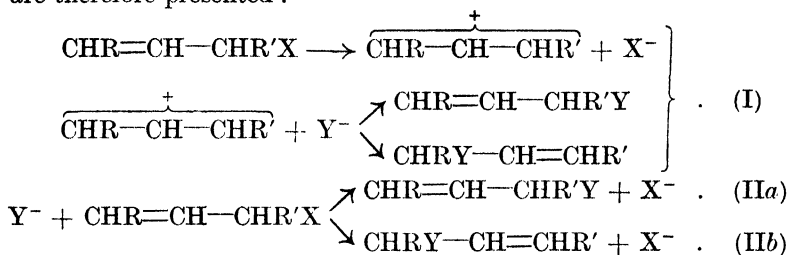
²⁵ *Trans. Faraday Soc.*, 1938, **34**, 194.

²⁶ See this Report, p. 211.

²⁷ *J.*, 1937, 207.

²⁸ See Hughes and Ingold's theory of the Walden inversion; this Report, p. 222.

addition of Y after the ionisation of X. The following possibilities are therefore presented : ²⁹



The analogy of these schemes with the two possible mechanisms of anionotropic change, and with the S_N1 and S_N2 mechanisms of aliphatic substitution is obvious. Since the formation of two isomeric substances by *either* mechanism cannot be excluded, the isolation of a mixed product ³⁰ may not be proof of the intermediate formation of a carbon cation, and the same remark applies to observations of simultaneous substitution and anionotropic change.³¹ Evidence in favour of the occurrence of substitution by mechanism II (in addition to mechanism I) is provided by W. G. Young and J. F. Lane's observation that the reactions of hydrogen bromide under standardised conditions with CHMe·CH·CH₂·OH and with CHMe(OH)·CH·CH₂ give mixed products containing different proportions of the isomeric bromides ; ²⁹ if the substitution occurred by

the ionisation mechanism alone, the mesomeric ion $\overline{\text{CHMe}\cdot\text{CH}\cdot\text{CH}_2}^+$ would be formed initially in each case, and identical products would be expected from the two isomeric alcohols. Substitutions by the mechanisms I and II will be unimolecular and bimolecular respectively; in agreement with this, J. Meisenheimer and G. Beutter ³² have found that the reaction of cinnamyl chloride with potassium acetate gives second-order kinetics in acetic anhydride medium, but in acetic acid the kinetics are between first and second order (a mixed product was obtained in the latter case only).

J. Kenyon and his collaborators have observed a pronounced loss of optical activity in a number of replacements of the anionic group of optically active derivatives of allyl alcohol ; ³³ *e.g.*, the replacement of the -O·CO·C₆H₄·CO₂H group of αγ-dimethylallyl hydrogen phthalate to give the formate, acetate or methyl ether. A more detailed study was made of the hydrogen phthalate and

²⁹ C. L. Arcus and J. Kenyon, *J.*, 1938, 1912; W. G. Young and J. F. Lane, *J. Amer. Chem. Soc.*, 1938, **60**, 847; E. D. Hughes, *ref.* 25.

³⁰ C. Prévost, *Compt. rend.*, 1928, **187**, 1052.

³¹ H. Burton, *J.*, 1928, 1650.

³² *Annalen*, 1933, **508**, 58.

³³ H. W. J. Hills, J. Kenyon, and H. Phillips, *J.*, 1936, 576; J. Kenyon, S. M. Partridge, and H. Phillips, *ref.* 27; C. L. Arcus and J. Kenyon, *ref.* 29.

chloride of γ -methyl- α -n-propylallyl alcohol, $\text{CHMe}:\text{CH}\cdot\text{CHPr}^{\alpha}\text{X}$. In the case of the hydrogen phthalate, formic or benzoic acid gave an inactive product, and acetic acid also brought about racemisation but with some retention of optical activity (inverted configuration); the chloride gave an inactive product with acetate ions, and mainly racemisation but a small retention of activity (again inverted configuration) when converted into the alcohol (by aqueous sodium carbonate) or the methyl ether (by potassium carbonate in methyl alcohol). The residual optical activity was in each case due to a derivative of the original γ -methyl- α -propyl compound, and never to its anionotropic (α -methyl- γ -propyl) form, as indicated by the complete inactivity of its reduction product [which for γ -methyl- α -propyl would be inactive CHPr_2X and for α -methyl- γ -propyl would be active $\text{CHMe}(\text{C}_5\text{H}_{11})\text{Y}$]. Arcus and Kenyon consider that the replacement occurs principally by the ionic mechanism (I), which would lead to racemisation, and the small preservation of optical activity is attributed either to some reaction by a bimolecular mechanism (IIa) or to a shielding of one side of the α -carbon atom by the receding anion.³⁴

It is remarkable that the alkaline hydrolysis of γ -phenyl- α -methylallyl, α , γ -dimethylallyl and γ -methyl- α -n-propylallyl hydrogen phthalates by concentrated (5N) sodium hydroxide gives an almost quantitative preservation of the original configuration;³⁵ decrease in the concentration or strength of the base leads to increasing racemisation. Arcus and Kenyon suggest a simple explanation. In neutral solution, the hydrogen phthalate exists largely as the undissociated ester-acid $\text{CHR}:\text{CH}\cdot\text{CHR}'\cdot\text{O}\cdot\text{CO}\cdot\text{C}_6\text{H}_4\cdot\text{CO}_2\text{H}$, and the anionisation of the group $\text{O}\cdot\text{CO}\cdot\text{C}_6\text{H}_4\cdot\text{CO}_2\text{H}$ is facilitated by the electron-attractive character of carboxyl, by the capacity for electron-release possessed by the double bond, and by the electron-repulsion of the alkyl groups R and R' (and still more by phenyl). But in strongly alkaline solution the entity concerned is the ion

$\text{CHR}:\text{CH}\cdot\text{CHR}'\overset{(a)}{\underset{(b)}{\text{O}}}\cdot\text{CO}\cdot\text{C}_6\text{H}_4\cdot\text{CO}_2^-$, and the electron repulsion of the negative pole, by opposing the fission of the molecule at (a), causes the hydrolysis to proceed by the normal mechanism,³⁶ which involves fission at (b) with elimination of $\text{CHR}:\text{CH}\cdot\text{CHR}'\cdot\text{O}-$ as an anion. The linkages of the asymmetric carbon atom are not here disturbed, and hence the stereochemical configuration is retained.

H. B. W.

³⁴ Compare p. 223.

³⁵ J. Kenyon, S. M. Partridge, and H. Phillips, *J.*, 1936, 85; H. W. J. Hills, J. Kenyon, and H. Phillips, ref. 33; C. L. Arcus and J. Kenyon, ref. 29.

³⁶ M. Polanyi and A. L. Szabo, *Trans. Faraday Soc.*, 1934, 30, 508. The corresponding mechanism for esterification has recently been demonstrated by I. Roberts and H. C. Urey (*J. Amer. Chem. Soc.*, 1938, 60, 2391).

3. INFLUENCES OF GROUPS UPON REACTIVITY.

Modern views concerning the nature of the influences which substituent atoms and groups exert upon the reactions of organic compounds are based upon the electronic theory of valency, and their progress has therefore gone hand in hand with the development of that theory. But the theoretical superstructure which has been erected has a broad foundation of experimental observations, which include, *inter alia*, comparisons of reaction velocities, measurements of the dissociation constants of acids and bases, determinations of the proportions of isomeric products (especially in aromatic substitution), and, of late years, the study of spectroscopic and other physical properties, notably the dipole moment. Some of the more important of the many recent contributions to the general problem are summarised below, and certain cases of a special character are then considered.

The General Problem from the Standpoint of Reaction Kinetics.—The vast majority of kinetic measurements have been conducted in solution, and simple comparisons of reaction velocities under fixed conditions have led, in the past, to important conclusions; in conjunction with other evidence they have given, for example, the familiar "polar sequence" $\text{NO}_2 > \text{Hal} > \text{H} > \text{Alkyl}$ for electron-attractive character. It has now become clear, however, that the mere comparison of velocity coefficients at a single temperature does not extract in full measure the information which a study of reaction speeds is capable of yielding, and it may, indeed, lead to wrong conclusions.* The measured velocity indicates the resultant effect of more than one factor, and the kinetic study of the reaction is not complete until some further analysis has been made. The kinetic equation $k = PZe^{-E/RT}$, where E is the energy of activation, Z is the collision frequency, and P denotes the proportion of sufficiently energised collisions which actually leads to the formation of the reaction products, provides a simple physical picture of the inner mechanism of the change, and its use has been abundantly justified by C. N. Hinshelwood.¹ Since it may be assumed that Z does not vary to any great extent from reaction to reaction, changes in velocity may be due to variations in E , in P , or in both. For reactions which have been studied kinetically, the values of E cover a range of many thousand calories, and P varies over about twelve powers of 10; these parameters frequently rise

¹ *J.*, 1937, 635; *Trans. Faraday Soc.*, 1938, 34, 105.

* The results of E. W. Timm and C. N. Hinshelwood (ref. 10) upon the acid-catalysed hydrolysis of the chloroacetic esters provide a particularly instructive example.

or fall simultaneously when the medium² or the pressure³ changes, and in a catalysed reaction P increases very considerably on passing from an uncharged to a charged catalyst.⁴ A number of factors which may influence the value of P have been enumerated by C. N. Hinshelwood and C. A. Winkler.⁵

One method of studying the influences of substituent groups is to determine the values of E and P , to as high a degree of approximation as is possible,* when each member of a series of compounds differing only in one group takes part in a given reaction. Two cases can here be distinguished; the variable substituent may be (a) well removed from the point of reaction, when local disturbances will be eliminated, or (b) quite close to the reactive centre.

In a number of instances of the former type, it has been shown that changes in velocity are due almost entirely to variations in the energy of activation, any variations in the value of P being insignificant. The most convenient series of reactions for study are those of benzene derivatives with a variable substituent placed m or p to the point of reaction, and the cases which have been investigated include the following: chlorination of phenolic ethers,⁶ benzylation of anilines,⁷ alkaline hydrolysis of benzoic esters,⁸ and the reaction of methyl iodide with dimethylanilines.⁹ Very considerable changes in E , leading to large differences in velocity, are accompanied in these examples by almost negligible variations in the value of P ,† and it would appear justifiable to conclude that,

² R. A. Fairclough and C. N. Hinshelwood, *J.*, 1937, 538, 1573; 1938, 236; C. N. Hinshelwood, *Trans. Faraday Soc.*, 1938, **34**, 138. A correlation of $\log PZ$ with $1/\sqrt{E}$ is suggested from theoretical considerations.

³ M. W. Perrin, *Trans. Faraday Soc.*, 1938, **34**, 144.

⁴ G. F. Smith, *J.*, 1934, 1744; A. T. Williamson and C. N. Hinshelwood, *Trans. Faraday Soc.*, 1934, **30**, 1145; C. N. Hinshelwood and A. R. Legard, *J.*, 1935, 587.

⁵ *J.*, 1936, 371.

⁶ A. E. Bradfield and B. Jones, *J.*, 1928, 1006, 3073; A. E. Bradfield, W. O. Jones, and F. Spencer, *J.*, 1931, 2907; A. E. Bradfield, *Chem. and Ind.*, 1932, **51**, 254.

⁷ E. G. Williams and C. N. Hinshelwood, *J.*, 1934, 1079.

⁸ C. K. Ingold and W. S. Nathan, *J.*, 1936, 222; D. P. Evans, J. J. Gordon, and H. B. Watson, *J.*, 1937, 1430.

⁹ K. J. Laidler, *J.*, 1938, 1786.

* The accuracy with which these values can be determined is not high, and is subject to some uncertainty. Caution should therefore be exercised before significance is attached to *small* differences (compare E. D. Hughes, C. K. Ingold, and U. G. Shapiro, *J.*, 1936, 228). V. K. LaMer and (Miss) M. L. Miller (*J. Amer. Chem. Soc.*, 1935, **57**, 2674) find indications of substantial variations of E and P with temperature in certain cases; the possibility of changes in reaction mechanism should not be overlooked, however.

† This is shown conveniently by plotting $\log_{10}k$ against E . It follows from the kinetic equation that, if PZ remains constant, the graph will be a

as a general rule, a substituent occupying a position which is well removed from the point of reaction influences the velocity almost entirely by its effect upon the energy of activation; E is raised or lowered according to the nature of the reaction and of the group. There are certain instances, however, in which appreciable changes in P are caused by substituents in the *m*- or *p*-positions. The most notable are the acid hydrolysis of benzoic esters,¹⁰ the alcoholysis of benzoyl chlorides,¹¹ and the hydrolysis of arylsulphuric acids;¹² P here increases or decreases with E , but its effect is never sufficiently great to outweigh the variations in the energy of activation, and these reactions may possess some complicating feature to which the changes in P are to be ascribed.¹³ The kinetic study of the acid hydrolysis of benzoic esters has revealed another interesting fact; like alkaline hydrolysis, it is favoured by electron-attractive substituents, whereas the reverse would have been anticipated. C. N. Hinshelwood, K. J. Laidler, and E. W. Timm¹⁴ conclude that the step which governs the value of E is the attack of a water molecule upon the carbonyl carbon; since, in the acid-catalysed reaction, this involves the removal of hydroxyl ions from water molecules, whereas in alkaline hydrolysis these ions are already present in high concentration, the energy of activation is considerably higher (by 5000—7000 cal.) in the former case than in the latter.¹⁵

Variation of a substituent group standing in close proximity to the point of reaction generally causes simultaneous variations in E and P ; this has been demonstrated in the esterification reactions of aliphatic acids,¹⁶ the addition of alkyl halides to tertiary bases,¹⁷ and in reactions of aromatic compounds having groups in the *o*-position.¹⁸

In a theoretical consideration of the factors which determine the energy of activation, C. N. Hinshelwood, K. J. Laidler, and E. W. Timm¹⁴ arrive at the conclusion that "there should be a general tendency for the influence of the substituent on the activa-

¹⁰ E. W. Timm and C. N. Hinshelwood, *J.*, 1938, 862.

¹¹ G. E. K. Branch and A. C. Nixon, *J. Amer. Chem. Soc.*, 1936, **58**, 2499.

¹² G. N. Burkhardt, C. Horrex, and (Miss) D. I. Jenkins, *J.*, 1936, 1649.

¹³ Compare D. P. Evans, V. G. Morgan, and H. B. Watson (*J.*, 1935, 1167) on the bromination of nuclear-substituted acetophenones where *small*, but regular, variations in P are observed.

¹⁴ *J.*, 1938, 848.

¹⁵ W. B. S. Newling and C. N. Hinshelwood, *J.*, 1936, 1357.

¹⁶ C. N. Hinshelwood and A. R. Legard, ref. 4.

¹⁷ C. A. Winkler and C. N. Hinshelwood, *J.*, 1935, 1147.

¹⁸ See p. 244.

straight line of slope $-2.303RT$, while a greater or smaller slope indicates an increase or decrease in PZ , which it is doubtless justifiable to attribute to variation in P rather than in the collision frequency Z .

tion energy to follow the direction indicated by its effect on the attraction of the reagent to the seat of reaction." This is found, of course, in a large majority of instances. Circumstances are envisaged, however, in which the effect of the substituent upon the bond which is to be ruptured will become of increasing importance and may take control; aliphatic substitution by the unimolecular mechanism might perhaps be regarded as an extreme instance of this kind, for the reagent is here not concerned in the rate-determining stage.¹⁹

Reference was made in last year's Report²⁰ to the linear relationship, noted by L. P. Hammett²¹ and by G. N. Burkhardt,²² which frequently exists between the logarithms of the velocity coefficients for different reactions of similarly constituted compounds, or between the logarithms of the velocity coefficients and those of the dissociation constants of the appropriate substituted acids or bases. For a series of *m*- or *p*-substituted aromatic compounds, where *P* does not vary (and it is to such compounds that most of the observed linear relationships refer), the variations in $\log k$ are a measure of changes in the energy of activation, while those in $\log K$ are a measure of differences in the free energy of ionisation. The relationship may therefore be written $\Delta E_1 = \alpha \Delta E_2$, where ΔE_1 and ΔE_2 are the changes in *E* caused by any given substituent (*i.e.*, the differences of the *E* values for the substituted and the unsubstituted compound) in the two processes.²³ This means that, for different substituents, a constant fraction of the effect is transmitted through a given structure.²⁴ A linear relationship is to be anticipated only when the effect of the group in the different systems involves the operation of the same factors, and when similar paths are available for its transmission (as in benzoic and cinnamic esters, for instance);²⁵ these limitations arise from the time-variable nature of certain electronic effects and the necessity for a conjugated system to make possible the transmission of effects by the tautomeric mechanism. Hinshelwood describes α as the "transmission coefficient". Hammett analyses the observed effect on the basis of

¹⁹ See this Report, p. 211.

²⁰ *Ann. Reports*, 1937, **34**, 52.

²¹ L. P. Hammett and H. L. Pfluger, *J. Amer. Chem. Soc.*, 1933, **55**, 4079; L. P. Hammett, *Chem. Reviews*, 1935, **17**, 125; *J. Amer. Chem. Soc.*, 1937, **59**, 96; *Trans. Faraday Soc.*, 1938, **34**, 158.

²² *Nature*, 1935, **136**, 684; G. N. Burkhardt, W. G. K. Ford, and E. Singleton, *J.*, 1936, 20.

²³ C. N. Hinshelwood, *J.*, 1937, 640; E. Tommila and C. N. Hinshelwood, *J.*, 1938, 1801.

²⁴ C. N. Hinshelwood, *Trans. Faraday Soc.*, 1938, **34**, 172.

²⁵ J. F. J. Dippy and H. B. Watson, *J.*, 1936, 436; H. B. Watson, *Trans. Faraday Soc.*, 1938, **34**, 174.

the equation $\Delta \log k = \sigma \rho$, where σ is a "substituent constant" dependent upon the nature of the group, and ρ a "reaction constant" dependent upon the reaction and the external conditions.

The General Problem from the Standpoint of the Electronic Theory of Valency.—Four distinct polar effects of groups are now recognised.²⁶ Two are polarisations (permanent effects), viz., (1) the inductive effect and (2) the mesomeric effect, and two polarisabilities (time-variable), viz., (3) the inductomeric effect and (4) the electromeric effect. Of these effects, (1) and (3) do not involve covalency changes and are capable of transmission through saturated systems. Effects (2) and (4) operate by the tautomeric mechanism, and, since they involve covalency changes, can be transmitted only in conjugated systems; they depend upon the phenomenon of quantum-mechanical resonance.²⁷

The classical dissociation constants of carboxylic acids, determined by Ostwald and others, have long been employed as criteria of the polar influences of substituents. A number of accurate thermodynamic constants have been obtained during recent years, in most cases for isolated acids. J. F. J. Dippy and his collaborators,²⁸ using an expeditious conductometric method, have now determined values for the thermodynamic constants of a large number of acids, principally of the benzoic, phenylacetic, β -phenylpropionic and cinnamic series, in aqueous solutions at 25°. These values are strictly comparable, and provide data from which the effects of groups in aromatic combination may be deduced with a good degree of certainty. Certain saturated and olefinic acids are also included. Dippy finds that the dissociation constants of the *m*-substituted acids in the benzoic, phenylacetic and β -phenylpropionic series show a linear relationship with the dipole moments of the corresponding substituted benzenes. This is quite distinct from the earlier correlation of $\log K$ with μ .²⁹ Further justification has been found for the use of dissociation constants referring to a single solvent and a single temperature in deducing the order of acid

²⁶ See R. Robinson, "Outline of an Electrochemical (Electronic) Theory of the Course of Organic Reactions," Institute of Chemistry, 1932; *J. Soc. Dyers and Colorists*, Jubilee Issue, 1934, p. 65; C. K. Ingold, *Chem. Reviews*, 1934, **15**, 225.

²⁷ See N. V. Sidgwick, *Ann. Reports*, 1934, **31**, 37; *J.*, 1936, 533; 1937, 694; C. K. Ingold, ref. 26; *J.*, 1933, 1120.

²⁸ J. F. J. Dippy and F. R. Williams, *J.*, 1934, 161, 1888; 1935, 343; J. F. J. Dippy, H. B. Watson, and F. R. Williams, *ibid.*, p. 346; J. F. J. Dippy and R. H. Lewis, *J.*, 1936, 644; 1937, 1008, 1426; J. W. Baker, J. F. J. Dippy, and J. E. Page, *J.*, 1937, 1774; J. F. J. Dippy and J. E. Page, *J.*, 1938, 357; J. F. J. Dippy, *J.*, 1938, 1222.

²⁹ W. S. Nathan and H. B. Watson, *J.*, 1933, 890; J. F. J. Dippy and H. B. Watson, ref. 25; H. B. Watson, *Trans. Faraday Soc.*, 1938, **34**, 165.

strengths; for example, a series of acids stand in the same order in *n*-butyl alcohol or chlorobenzene as in water,³⁰ and the sequence appears to remain when the temperature is changed.³¹ Of recent studies of the strengths of bases, the most extensive is that of N. F. Hall and M. R. Sprinkle.³²

Sutton's rule, which relates the differences between the dipole moments of aromatic compounds ArylX and of their aliphatic analogues AlkylX with the *op*- or *m*-directive influences of the groups X in aromatic substitution, has been confirmed by L. G. Groves and S. Sugden,³³ using new values for the dipole moments in the vapour state. The same authors have calculated the values of the mesomeric moments in substituted benzenes³⁴ (certain approximations and assumptions being necessary with regard to valency angles and induction within the molecule), and they find that, whereas *op*-directive groups give quite large mesomeric moments (*e.g.*, C_6H_5Cl 0.97, $C_6H_5\cdot OH$ 1.12 Debye units), those due to *m*-directive groups are small (*e.g.*, $C_6H_5\cdot NO_2$ 0.29, $C_6H_5\cdot COMe$ 0.17). R. J. B. Marsden and L. E. Sutton³⁵ find 1.55 d. for the mesomeric moment of NMe_2 , and the mesomeric effects of the sulphoxide, nitroso- and iodoxy-groups have been discussed by D. L. Hammick and R. B. Williams.³⁶ Comparison of the dipole moments of *p*-substituted phenols, phenolic ethers and anilines with those calculated by vector addition of the moments of the corresponding monosubstituted benzenes has revealed an appreciable difference between the two sets of values³⁷; in other words, the mesomeric effect of a group in aromatic combination is not a constant quantity, but is influenced by other groups present, and this may explain, *inter alia*, the deviation of *p*-substituted benzoic acids from the $\log K-\mu$ relationship which their *m*-isomerides obey.³⁸

The proportions of *o*-, *m*-, and *p*-isomerides formed in replacements

³⁰ L. A. Wooten and L. P. Hammett, *J. Amer. Chem. Soc.*, 1935, **57**, 2289; L. P. Hammett, *Trans. Faraday Soc.*, 1938, **34**, 162; D. C. Griffiths, *J.*, 1938, 818. Compare *Ann. Reports*, 1934, **31**, 79, and I. M. Kolthoff, J. J. Lingane, and W. D. Larson, *J. Amer. Chem. Soc.*, 1938, **60**, 2512.

³¹ L. P. Hammett, *J. Chem. Physics*, 1936, **4**, 613; cf. J. F. J. Dippy, *J.*, 1937, 1776.

³² *J. Amer. Chem. Soc.*, 1932, **54**, 3469.

³³ *J.*, 1935, 971.

³⁴ *J.*, 1937, 1992. These are based upon dipole moments in the vapour phase.

³⁵ *J.*, 1936, 599. They have also calculated values for NH_2 , OH , and OMe ; these are referred to later. All are based on dipole moments in benzene solutions.

³⁶ *J.*, 1938, 211.

³⁷ G. M. Bennett and S. Glasstone, *Proc. Roy. Soc.*, 1934, **A**, **145**, 71. Compare *Ann. Reports*, 1929, **26**, 132; Marsden and Sutton, ref. 35.

³⁸ H. B. Watson, ref. 29.

of nuclear hydrogen by electrophilic reagents have formed one of the foundation stones of the electronic theory of reactivity. The relative *velocities* of nitration (by acetyl nitrate in acetic anhydride) at the various positions in toluene,³⁹ ethyl benzoate⁴⁰ and the halogenobenzenes⁴¹ have now been determined. The *total* velocity (referred to that for unsubstituted benzene) was found by a competitive method, and by combining the figures so obtained with the proportions of the isomerides in the product, the "partial rate factors" for the *o*-, *m*- and *p*-positions (indicating their relative reactivities) were calculated. The results are summarised below :

Compound.	Partial rate factors.		
	<i>o</i> .	<i>m</i> .	<i>p</i> .
C_6H_6	1	1	1
$C_6H_5\cdot CH_3$	43	3	55
$C_6H_5\cdot CO_2Et$	0.0026	0.0079	0.0009
C_6H_5Cl	0.030	0.000	0.139
C_6H_5Br	0.037	0.000	0.106

The total rates of nitration of the halogenobenzenes were found to be as follows ($C_6H_6 = 1$): PhF 0.15, PhCl 0.033, PhBr 0.030, PhI 0.18. The sequence $H \gg I \sim F \gg Cl > Br$ has been confirmed by a dilatometric method.⁴² The results for toluene and ethyl benzoate are in accordance with expectation. The electron-repulsive methyl group makes all positions more reactive towards an electrophilic reagent, but the *o*- and *p*-positions far more so than the *m*-position; carbethoxyl, on the other hand, by reason of its electron-attractive character, deactivates all positions, again *o* and *p* more than *m*.

The new figures relating to the halogenobenzenes bring up again the vexed question of the effects of halogens when linked to the benzene nucleus. This has been discussed fully by G. Baddeley, G. M. Bennett, S. Glasstone, and B. Jones.⁴³ The observed effects of halogens in aliphatic compounds lead to the order $F > Cl > Br > I$ for their inductive effects. From their behaviour in aromatic compounds it is necessary to postulate also a mesomeric effect decreasing in magnitude in the same order, *viz.*, $F > Cl > Br > I$; this order was first suggested by G. Baddeley and G. M. Bennett,⁴⁴ and L. G. Groves and S. Sugden³⁴ have more recently found the following values (Debye units) for the mesomeric

³⁹ C. K. Ingold and (Miss) F. R. Shaw, *J.*, 1927, 2918; *Ann. Reports*, 1927, **24**, 152; C. K. Ingold, A. Lapworth, E. Rothstein, and D. Ward, *J.*, 1931, 1959; *Ann. Reports*, 1931, **28**, 115.

⁴⁰ C. K. Ingold and (Miss) M. S. Smith, *J.*, 1938, 905.

⁴¹ (Miss) M. L. Bird and C. K. Ingold, *ibid.*, p. 918.

⁴² G. A. Benford and C. K. Ingold, *ibid.*, p. 929.

⁴³ *J.*, 1935, 1827.

⁴⁴ *J.*, 1933, 261. Compare G. M. Bennett, *ibid.*, p. 1112.

moments in the four halogenobenzenes: F 1, Cl 0.97, Br 0.89, I 0.87. The chemical evidence relating to the mesomeric effect is given in the paper by Bennett and his co-workers, who also discuss the origin of this effect. A polarisability of the halogen-nucleus bond, decreasing in the order $I > Br > Cl > F$, is also postulated; this may be either an inductomeric⁴³ or an electromeric⁴⁵ polarisability.

The replacement of nuclear hydrogen by deuterium is an electrophilic substitution, and is subject to the rules which govern other substitutions by electrophilic reagents. Thus, the effects of nuclear groups upon the speed of deuteration give the usual sequence $O^- > NMe_2 > OMe > H > SO_3H$,⁴⁶ and phenol and aniline are deuterated exclusively in the *o*- and *p*-positions.⁴⁷

ortho-Substituted Compounds.—N. V. Sidgwick and R. K. Callow's postulate⁴⁸ of a hydrogen bond in *o*-substituted phenols where the second group contains an electron-donating atom (*e.g.*, CHO, CO₂R, NO₂, Cl) and where the process "completes" a five- or more frequently a six-membered "chelate ring", has received abundant confirmation,⁴⁹ and the difficulty which once existed with respect to "two-covalent" hydrogen has now been removed.⁵⁰ The view has been applied by G. E. K. Branch and D. L. Yabroff⁵¹ to explain the unusually high dissociation constant of salicylic acid (as compared with the isomeric acids), and by W. Baker⁵² in connection with the further increase in strength brought about by the introduction of hydroxyl in the remaining *o*-position; if it be supposed that chelation occurs mainly in the anion (where it would be favoured by the negative charge), the resulting decrease in electron-availability of the carboxylate group accounts for the high strength. Recent confirmation of Sidgwick's view is found in observations of the Raman spectra of salicylaldehyde and ethyl salicylate,⁵³ and in the removal of marked differences in the behaviour of the stereoisomeric *o*-hydroxybenzophenoneoximes by acylation of the phenolic hydroxyl or by salt formation.⁵⁴

⁴⁵ A. E. Oxford and R. Robinson, *J.*, 1927, 2239; R. Robinson, *J.*, 1933, 1114; Bird and Ingold, *ref.* 41; J. W. Baker, *J.*, 1936, 1448.

⁴⁶ C. K. Ingold, C. G. Raisin, and C. L. Wilson, *J.*, 1936, 1637.

⁴⁷ A. P. Best and C. L. Wilson, *J.*, 1938, 28.

⁴⁸ *J.*, 1924, 125, 527; *Ann. Reports*, 1924, 21, 104.

⁴⁹ See summaries by E. N. Lassettre, *Chem. Reviews*, 1937, 20, 259, and W. Baker, *Ann. Reports*, 1936, 33, 283.

⁵⁰ *Ann. Reports*, 1933, 30, 112; 1934, 31, 40.

⁵¹ *J. Amer. Chem. Soc.*, 1934, 56, 2568.

⁵² *Nature*, 1936, 137, 236.

⁵³ L. Kahovec and K. W. F. Kohlrausch, *Z. physikal. Chem.*, 1937, B, 38, 119.

⁵⁴ A. H. Blatt, *J. Amer. Chem. Soc.*, 1938, 60, 205.

Internal hydrogen-bond formation is not restricted to phenolic compounds. The work of von Auwers and others has shown that amides and anilides are normally associated in solution, but that there is little or no association in anilides having a nitro- or aldehydo-group in the *o*-position (a similar lack of association occurs when both amide hydrogens are replaced, for no hydrogen is then available for bond formation). H. O. Chaplin and L. Hunter⁵⁵ have now demonstrated the absence of molecular association in a further number of compounds where an electron-donating group is situated in the *o*-position with respect to an acylamido-group; they include *o*-nitroacylanilides, *o*-acetamidoazo-compounds, ethyl *o*-acetamidobenzoate, *o*-acetamidoacetophenone, 1-acetamidanthraquinone and 8-acetamidoquinoline. The authors interpret this lack of association by postulating a hydrogen linkage between the nitrogen of the amide group and a suitably placed atom of electron-donating character (O of CO₂Et, COR or NO₂; N of N:NAr or quinoline). Extension of this work has indicated, however, that such chelation is greatly reduced by the presence of an additional group in either the 6-position or the 3-position (this "group" may be the second nucleus of a naphthalene derivative). This occurs, for example, if CH₃, Br or NO₂ is introduced into the 6-position in *o*-nitroacetanilide, and, of the isomeric compounds (I) and (II), (I) shows considerable association and (II) does not [*i.e.*, (I) is not chelated]. Chelation



is similarly reduced by the presence of a group (NO₂, CH₃, CO₂Et, Br) in the 3-position in *o*-nitroacetanilide, but introduction of Br or CH₃ (OEt is ineffective) into position 4 in 2 : 3-dinitroacetanilide results in *increased* chelation. These phenomena are attributed to steric interference by the group in the 6- or the 3-position; the authors suggest that the acetamido-group or the *o*-substituent is thereby excluded from the plane of the benzene nucleus, and it will then be difficult for these groups to position themselves suitably for hydrogen-bond formation. A group in position 4 will have a similar steric effect upon one in position 3, however, and so prevent it from exerting its full effect. At the same time, of course, the mutual interaction of these groups occupying adjacent positions is not impossible.

The considerable evidence of chelation in compounds where two groups stand in *o*-positions with respect to each other suggests the possibility that similar processes may contribute to the familiar

⁵⁵ *J.*, 1937, 1114; 1938, 375, 1034.

unreactivity of many *o*-substituted benzene derivatives. It has long been realised that the Victor Meyer conception of steric retardation by a purely geometrical effect is not capable of embracing all the facts, and the necessity for some additional or alternative explanation has been emphasised by the observation that "steric hindrance" is in some cases associated with a high energy of activation. For instance, D. H. Peacock⁵⁶ has found that the values of *E* for the reactions of *o*-toluidine with benzyl chloride and 2 : 4-dinitrochlorobenzene are distinctly higher than the corresponding values relating to *m*- and *p*-toluidines, and C. N. Hinshelwood and A. R. Legard's study of the esterification of *o*-nitrobenzoic and *s*-trimethylbenzoic acids⁴ has revealed a considerable increase in *E* and also a rise in the value of *P* due to the presence of the groups in *o*-positions. A purely geometrical effect would lead to a low velocity by reducing *P* rather than by increasing *E*.

The *ortho*-effect appears to operate only when the reacting group contains an electron-donating atom (*e.g.*, NR₂, COR, CO₂R). Thus, it is manifested in the reactions of benzoyl chlorides but not in those of benzyl chlorides;⁵⁷ *o*-substituted phenols do not appear to exhibit such an effect, and it may be noted in this connection that imino-ethers (with C—OR) differ from the isomeric amides (with C=O) in that they are not associated.⁵⁸ A kinetic study of the alkaline hydrolysis of *o*-substituted benzoic esters⁵⁹ has indicated a further necessary condition: the substituent must be capable of acting as electron-acceptor. With nitroxyl, chlorine or methyl in the *o*-position the hydrolysis is relatively slow, the low velocity being due to a reduction of the *P* factor (as compared with its value for the unsubstituted, *m*-substituted or *p*-substituted esters) by about a power of 10; the values of *E* are slightly less than those for the isomeric *p*-substituted esters. The three groups referred to may all be regarded as possible electron-acceptors; chlorine on the basis of Sidgwick's covalency rule, nitroxyl on grounds put forward by G. M. Bennett and G. H. Willis,⁶⁰ and methyl by virtue of an ability to form a hydrogen bond under favourable conditions (such a linkage was suggested tentatively by Sidgwick and Callow for *o*-nitrotoluene, and other possible examples are discussed later⁶¹). Fluorine, however, presents an instance where the acceptance of electrons is definitely impossible (it cannot expand its valency group

⁵⁶ *Nature*, 1932, **129**, 57; A. Singh and D. H. Peacock, *J. Physical Chem.*, 1936, **40**, 669.

⁵⁷ S. C. J. Olivier, *Rec. Trav. chim.*, 1929, **48**, 227; 1930, **49**, 697. Compare G. M. Bennett and B. Jones, *J.*, 1935, 1815.

⁵⁸ H. O. Chaplin and L. Hunter, *J.*, 1937, 1114.

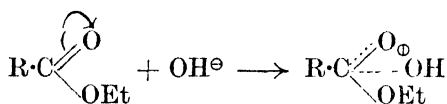
⁵⁹ D. P. Evans, J. J. Gordon, and H. B. Watson, *ref.* 8.

⁶⁰ *J.*, 1929, 256.

⁶¹ See p. 250.

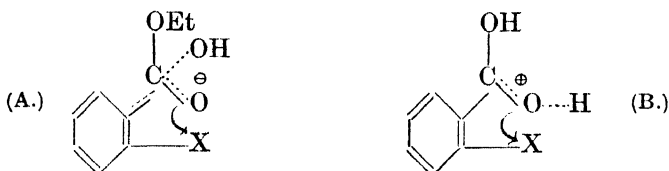
beyond eight), and in ethyl *o*-fluorobenzoate the criteria of the *ortho*-effect disappear completely; its behaviour is almost identical with that of the *p*-isomeride. The indications are, therefore, that the operation of the *ortho*-effect demands electron-donating and electron-accepting groups, and it is no great step to postulate interaction between these two groups to give either a co-ordinate bond or a hydrogen bond.⁶²

In the anilides and phenols to which reference has been made, there is evidence of chelation under ordinary conditions; this is, of course, to be attributed to the ionisable character of the hydrogen in the acylamino- or hydroxyl group. Ethyl salicylate is included in this category, but there is no reason whatsoever to suppose that the corresponding esters containing nitroxyl, halogen or methyl are chelated. The suggestion is therefore made that the interaction of groups to give a co-ordinate bond or a hydrogen bond occurs only *in the transition complex*. The first step in alkaline hydrolysis may be written



As the hydroxyl ion approaches, an electron-pair begins to recede from carbon, to come under the sole control of oxygen (which therefore acquires an increasing negative charge), and the system climbs the energy valley to the pass which represents the transition state. It is not improbable that, simultaneously with these processes, the unshared electrons of oxygen (now in relatively high energy levels) will interact with a suitably placed acceptor. If chelation does occur at this stage, the energy required for the formation of the transition complex is not likely to be affected to any great extent;

perhaps the electromeric change $\text{C}=\text{O} \rightleftharpoons \text{C}^\ominus-\text{O}^\ominus$ may be rendered rather



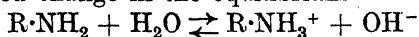
easier, in accordance with the slightly low value of *E*. But if the approaching reagent is an acid catalyst (as in esterification processes) which attacks the group at oxygen, the decreased electron availability of this atom will operate against reaction, and *E* will be

⁶² J. F. J. Dippy, D. P. Evans, J. J. Gordon, R. H. Lewis, and H. B. Watson, *J.*, 1937, 1421.

raised, as Hinshelwood and Legard found. The chelation processes for alkaline hydrolysis and acid-catalysed esterification are represented, on this view, by the curved arrows in (A) and (B).

It is clear that the effect of the process in either case is to transfer a negative charge from oxygen of carbethoxyl or carboxyl to the *o*-substituent, and the portion of the complex upon which the reaction depends is rendered *less negative* in (A) and *more positive* in (B); *i.e.*, in (A) it becomes *less* and in (B) *more* highly charged. Now it is well known that a relatively high *P* value is characteristic of reactions involving either an ion or a charged catalyst; the charge may make the complex more stable, so that it is better able to exist while the processes leading to the completion of the reaction are taking place (instead of falling apart to give the original reagents). The effect of chelation upon that part of the complex where these processes must occur is thus in the direction which will lead to a *lower P* factor in (A) and a *higher* value of *P* in (B), as is found experimentally. Alternatively it may be argued that the transfer of negative charge may lead to the less facile elimination of OEt from (A) and the more ready reaction of (B) with an alcohol molecule; again the change in *P* would be in the direction indicated by experiment, since the value of this factor will depend, *inter alia*, upon the proportion of the complexes which actually leads to products.*

The relatively high dissociation constants of *o*-substituted benzoic acids⁶³ may be due, in some cases, to chelation in the anion, as suggested by Branch and Yabroff for salicylic acid. This interpretation does not hold throughout, however, and other factors such as the bulk of the substituent doubtless intervene; in fact, steric hindrance of the Victor Meyer type can rarely be neglected as a possible contributory effect in considerations of the behaviour of *o*-substituted compounds. Groups in the *o*-positions decrease the strengths of bases; the position of the substituent is here not always suitable for a chelation process (*e.g.*, *o*-chloroaniline would require a four-membered ring, which is most unlikely), but it would appear, nevertheless, that the unshared electron pair of the nitrogen must be torn away from some constraint before the necessary union with a proton can occur. The reduced strength is not explicable on the basis of a bulk effect, which would operate unfavourably upon the reversed change in the equilibrium



(in dilute solution where the base is in constant contact with water molecules), thus giving an *increase* in strength; increased stability

⁶³ See table given by J. F. J. Dippy and R. H. Lewis, *J.*, 1937, 1426.

* On this point, see H. B. Watson, "Modern Theories of Organic Chemistry," Oxford University Press, 1937, p. 161.

of the hydroxide is not impossible in view of the effect of *o*-substituents upon benzaldehydecyanohydrins.⁶⁴

W. C. Davies and H. W. Addis⁶⁵ find that dimethyl-*o*-toluidine is actually stronger than its *p*-isomeride (although *o*-toluidine is weaker than *p*-), whereas an *ortho*-effect is indicated in its reactions with alkyl halides. If NMe₂ has a greater mesomeric effect than NH₂ (as the electron-repulsive character of the methyl groups makes probable, and as is indicated by the values of the dipole moments of aniline and dimethylaniline⁶⁶), this will render the protons of the *o*-methyl group less reactive, but they may nevertheless interact in some way with the unshared electrons of the nitrogen in a highly energised transition complex.

Alkyl Groups.—The absence of a dipole moment in all paraffins makes it necessary to suppose that alkyl groups exert only those polar effects which are impressed on them by other groups present in the molecule.⁶⁷ Since the substituents commonly encountered are attractors of electrons, alkyl groups normally exhibit a rather feeble electron repulsion, but it is not impossible that they might in certain circumstances display the opposite effect.*

The electron-repulsive characters of alkyl groups should increase in magnitude as the *n*-series is ascended (Me < Et < Pr^a < Bu^a, etc.), and also in series such as Me < Et < Pr^β < Bu^γ, for the higher groups are all derived from the lower by successive replacements of H by CH₃. This sequence is found in a number of instances which have been enumerated in recent papers.^{68, 69} In the *n*-series the differences become smaller as the length of the chain increases, and the dipole moments of homologous alkyl halides and other compounds have been found to reach a constant value at an early stage in the series (*e.g.*, at Pr^a for chlorides and bromides

⁶⁴ A. Lapworth and R. H. F. Manske, *J.*, 1928, 2546.

⁶⁵ *J.*, 1937, 1622.

⁶⁶ Recent values for the vapours are PhNH₂ 1.48 and PhNMe₂ 1.61 D. (L. G. Groves and S. Sugden, *J.*, 1937, 1782). Using values for benzene solutions, R. J. B. Marsden and L. E. Sutton (ref. 35) have calculated the mesomeric moments as PhNH₂ 1.12 and PhNMe₂ 1.55.

⁶⁷ C. K. Ingold, *Chem. Reviews*, 1934, 15, 238.

⁶⁸ E. E. Ayling, *J.*, 1938, 1014.

⁶⁹ D. P. Evans, J. J. Gordon, and H. B. Watson, *ibid.*, p. 1439.

* The mesomeric moments of phenol and anisole [1.12 and 0.40 D. respectively; Groves and Sugden (ref. 34), but Marsden and Sutton (ref. 35) calculate the reverse order, *viz.*, 0.84 and 1.03] and the relative strengths of certain hydroxy- and methoxy-substituted acids might indicate such a reversal of character when alkyl groups are linked to oxygen (the effect of increase in the size of the group is in the usual direction), but an interpretation of this kind (suggested by J. F. J. Dippy, *J.*, 1938, 1224) must at present be treated with reserve.

and at Bu^t for iodides ⁷⁰); a similar tendency to a constant value has frequently been observed in the effects of the groups upon chemical changes, and in the chlorination of a series of phenolic ethers $\text{RO}\cdot\text{C}_6\text{H}_4\text{X}$ an actual decrease in the effect is found when R reaches *n*-heptyl.⁷¹ If the alkyl group is removed some distance from the reactive centre, as, for example, by interposition of an aromatic nucleus, the differences become very small and are not easy to detect or to interpret with any degree of certainty; this has been found in some recent investigations,⁷² and it constitutes one of the difficulties which have been encountered in the study of the influences of alkyl groups.

In a large number of instances the observed effects of alkyl groups do not follow the theoretical order. These peculiarities are sometimes due to a change in reaction mechanism, and not to any abnormality on the part of the group itself,⁷³ and in such cases irregularity is observed only when primary groups are compared with secondary or tertiary, or secondary with tertiary, for all primary (secondary or tertiary) groups appear to give a reaction of the same mechanistic type. E. E. Ayling ⁶⁸ has suggested that *n*-alkyl groups show divergence from the theoretical sequence only when they are not themselves participating in the reaction but are exerting their influence upon the reacting group.

Two causes of abnormal behaviour have been suggested during recent years. J. W. Baker and W. S. Nathan ⁷⁴ have dealt with instances where methyl exhibits a capacity for electron release superior to that of higher groups; for example, in the nitration of *p*-alkyltoluenes substitution occurs predominantly *ortho* to the methyl group, and Baker and Nathan quote a number of other instances to which their view is applicable (*e.g.*, the singular lack of reactivity of some compounds containing the *isobutyl* group ⁷⁵). Briefly, the view is that the C—H electron pairs of methyl can come under the control of the adjacent nucleus, giving rise (in a conjugated system) to an effect which is superimposed upon and is of the same sign as the inductive effect; it is of a permanent character, and may accelerate or retard a chemical change, and its magnitude

⁷⁰ L. G. Groves and S. Sugden, *J.*, 1937, 158; E. G. Cowley and J. R. Partington, *J.*, 1938, 977.

⁷¹ B. Jones, *J.*, 1935, 1831. Compare *idem*, *J.*, 1936, 1854.

⁷² *E.g.*, *idem*, *J.*, 1938, 1414.

⁷³ See this Report, p. 212.

⁷⁴ *J.*, 1935, 1844. A rather similar suggestion was made by G. N. Burkhardt and M. G. Evans (*Mem. Manchester Lit. Phil. Soc.*, 1933, 77, 37, and quoted by G. N. Burkhardt, C. Horrex, and Miss D. I. Jenkins, *J.*, 1936, 1657).

⁷⁵ G. M. Bennett and F. M. Reynolds, *J.*, 1935, 131; B. V. Tronov and L. V. Ladigina, *Ber.*, 1929, 62, 2844; B. V. Tronov and N. C. Ssibgatullin, *ibid.*, p. 2850; W. C. Davies, *J.*, 1938, 1865.

decreases as the hydrogen atoms of methyl are replaced ($\text{Me} > \text{Et} > \text{Pr}^\beta$), becoming zero in *tert.*-butyl. The co-operation of such an effect with the inductive effect (which increases in magnitude from Me to Bu $^\gamma$) may account for the peculiar order of the dissociation constants of the *p*-alkylbenzoic acids ($\text{Me} < \text{Et} \sim \text{Pr}^\beta > \text{Bu}^{\gamma 76}$), for the order primary < secondary > tertiary for the strengths of aliphatic amines, and for the equality of the strengths of propionic and isobutyric acids.⁷⁷ A similar equality is found in the energies of activation for the alkaline hydrolysis of propionic and isobutyric esters, whereas the series of *n*-esters give results in accordance with the sequence of the inductive effects of the alkyl groups; ⁶⁹ the same influence can be traced in the acid-catalysed prototropy of the homologues of acetophenone.⁷⁸ In these cases the larger inductive effect of the secondary alkyl group appears to be balanced by its smaller electron-release by the Baker-Nathan mechanism.

The second suggestion has been made in order to account for peculiarities of a different type. In 1930, G. M. Bennett and A. N. Mosses ⁷⁹ postulated for the methyl group a direct polar effect of opposite sign to its inductive effect. This would, of course, have greatest influence at a point of the molecule which can approach the methyl group closely, and the rather high dissociation constant of *n*-butyric acid (as compared with propionic and *n*-heptoic acids) was cited as an example of its operation. The same view has recently been applied by E. E. Ayling ⁶⁸ to the explanation of a number of phenomena, including his own observations of the Hantzsch pyridine condensation; for a series of aliphatic aldehydes $\text{R}\cdot\text{CHO}$ the yield of product is unexpectedly high for $\text{R} = \text{Pr}^a$. In a study of the acid-catalysed prototropy of phenyl alkyl ketones, D. P. Evans ⁷⁸ has observed a notable rise in the energy of activation, and also an increase in the *P* factor, on passing from acetophenone to propiophenone; in actual magnitude the increase in *E* was twice as great as that found when a *p*-nitro-group was introduced into the nucleus, but further lengthening of the chain produced little effect. Evans has suggested that a hydrogen bond is formed, in the transition complex, between the carbonyl oxygen and the β -carbon atom of propiophenone and higher ketones. This is actually a modification (or perhaps a more precise definition) of the original view of Bennett

⁷⁶ J. W. Baker, J. F. J. Dippy, and J. E. Page, *J.*, 1937, 1774. The actual differences are small, but reasons are given for accepting them as real and significant.

⁷⁷ J. F. J. Dippy, *J.*, 1938, 1222. The possibility of an effect opposite in sign to the inductive effect and greatest in the tertiary group is suggested as an alternative to Baker and Nathan's view.

⁷⁸ D. P. Evans, *J.*, 1936, 785; D. P. Evans and J. J. Gordon, *J.*, 1938, 1434.

⁷⁹ *J.*, 1930, 2364.

and Mosses. It is in harmony with the fact that the values of E for the base-catalysed prototropy of the same ketones show no anomaly, but rise steadily in accordance with the inductive effects of the alkyl groups, whereas at propiophenone there is a decrease in the value of P ; the position is here similar to that found in the alkaline hydrolysis of *o*-substituted benzoic esters,⁸⁰ and the analogy extends further, for, in the hydrolysis of a series of aliphatic esters, a fall in P is observed for ethyl *isobutyrate* and ethyl trimethylacetate.⁶⁹ Lapworth and Manske's dissociation constants of the cyanohydrins of phenyl alkyl ketones⁸¹ have also been discussed in the light of this view.

In an accurate redetermination of the dissociation constants of a series of aliphatic acids (up to *n*-nonoic) J. F. J. Dippy⁷⁷ finds that the values for *n*-butyric and the higher acids are displaced upwards as compared with those for acetic and propionic acids, and he considers that this is due to some degree of chelation in the anions of the former acids. The "chelate ring" which is "completed" by the hydrogen bond is here six-membered, as is that postulated, for example, in salicylic acid. The chelation suggested by Evans in the prototropy of ketones (and the hydrolysis of aliphatic esters) leads to a "five-membered ring," on the other hand. The contradiction is only apparent, however, since the "chelate rings" contain different numbers of double linkages, and the electron-donating atom will interact with the hydrogen atom most favourably placed.

The above suggestions appear to embrace a considerable proportion of the instances where alkyl groups place themselves in an order different from that of their inductive effects. There are, however, certain observations which do not admit of interpretation along these lines. One obvious case is the abnormal basic strength of diethylaniline, and the same peculiar effect of two ethyl groups appears in the very high energy of activation for the alkaline hydrolysis of diethylacetic ester.⁶⁹ This effect is quite unexplained. The order of strengths of the *p*-alkyldimethylanilines⁸² also seems to defy interpretation.

H. B. W.

4. FATTY ACIDS AND OTHER LONG-CHAIN COMPOUNDS.

Methods of Synthesis and Preparation.—The outstanding advance in methods of building up paraffinoid chains is the modification¹

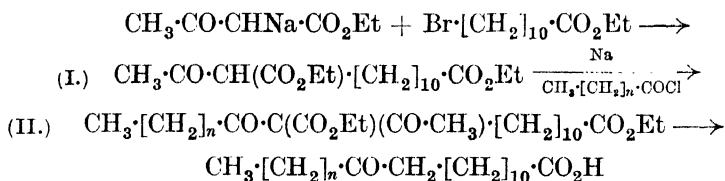
⁸⁰ See this Report, p. 245.

⁸² W. C. Davies, ref. 75.

⁸¹ J., 1930, 1976.

¹ (Mrs.) G. M. Robinson, J., 1930, 745.

of the Robinson synthesis² of keto-acids. In its present form the synthesis involves the following stages :



Ethyl α -acetylbrassyate (I) is obtained in good yield from the readily available 11-bromoundecic ester.^{3, 6} The complex (II) resulting from the condensation of the sodio-derivative of (I) with an acid chloride is submitted to a graded hydrolysis and yields the long-chain keto-acid, accompanied by varying amounts of 13-ketotetradecic acid. These higher keto-acids are readily reduced by the Clemmensen⁴ method, and thus twelve carbon atoms are added at a time to the original acid (or acid chloride). Stearic acid yields *n*-triacontanoic acid,⁵ undecic and lauric acids yield tri-cosanoic and tetracosanoic acids respectively.⁶ Starting from behenoyl chloride, tetratriacontanoic acid and then hexatetracontanoic acid ($\text{C}_{46}\text{H}_{92}\text{O}_2$) were synthesised.⁷ 15-Phenylpentadecic acid and 22-phenylbehenic acid⁸ and also ketones, *e.g.*, 12-nonacosanone,⁹ have been made, the last by a modification of the process. Another modification led to the synthesis at the Culion Leper Colony of *dl*-chaulmoogric acid.¹⁰

The alcohols from decanol to octadecanol are now commercial products, but even the "purest" grades need much further purification.¹¹ Paraffins have been made readily accessible by modifications in the methods of reducing the iodides.¹²

Purification.—In 1898, L. E. O. de Visser¹³ at the Apollo Candle

² (Mrs.) G. M. Robinson and R. Robinson, *J.*, 1925, **127**, 175; 1926, 2204; *Ann. Reports*, 1925, **22**, 80.

³ R. Ashton and J. C. Smith, *J.*, 1934, 435, 1308.

⁴ E. Clemmensen, *Ber.*, 1913, **46**, 1837; H. R. Le Sueur and J. C. Withers, *J.*, 1915, **107**, 736.

⁵ (Mrs.) G. M. Robinson, *J.*, 1934, 1543.

⁶ R. Ashton, R. Robinson, and J. C. Smith, *J.*, 1936, 283.

⁷ F. Francis, (Miss) A. M. King, J. A. V. Willis, and F. J. E. Collins, *J.*, 1937, 999.

⁸ G. M. Hills and R. Robinson, *J.*, 1936, 281.

⁹ S. H. Piper, A. C. Chibnall, S. J. Hopkins, A. Pollard, J. A. B. Smith, and E. F. Williams, *Biochem. J.*, 1931, **25**, 2072.

¹⁰ G. A. Perkins and A. O. Cruz, *J. Amer. Chem. Soc.*, 1927, **49**, 1070; *Ann. Reports*, 1927, **24**, 88.

¹¹ J. W. C. Phillips and S. A. Mumford, *J.*, 1933, 235; 1934, 1657.

¹² (Miss) P. C. Carey and J. C. Smith, *J.*, 1933, 346.

¹³ *Rec. Trav. chim.*, 1898, **17**, 182.

Works, Schiedam, crystallised stearic acid fifty-one times and palmitic acid thirty-six times from alcohol. Actually such a procedure was not sufficiently varied, and his products were slightly contaminated probably with each other and with traces of ethyl esters; but de Visser set a standard which has not often been reached, and in this field of higher aliphatic compounds physical chemists have really merited the gibe of making very accurate measurements on very impure substances. The main difficulty lies in separating substances from the homologues with which they are usually associated and with which they form solid solutions. Another factor is that, as the binary systems on pages 261—262 show, the depressions of melting point by admixture with homologues are small. Carboxylic acids show relatively large depressions, yet 1 % of palmitic acid lowers the melting point of stearic acid by only 0.24° ; ¹³ as an extreme example the addition of 20 molecules % of tetracosanoic acid to tricosanoic acid lowers the melting point by only 0.45° ; ⁶ the melting point of a hydrocarbon is usually raised steadily by the addition of a higher homologue.

Temperatures should therefore be correct to $\pm 0.1^{\circ}$, preferably to $\pm 0.05^{\circ}$, which entails the use of 1—3 grams of the substance and a standardised thermometer *in the liquid*. For pure substances the melting point and freezing point then differ by less than 0.05° , unless there is a transition near the melting point.¹⁴

When only small amounts of substance are available, the procedures described by Chibnall ⁹ or by F. Francis and F. J. E. Collins,¹⁵ using capillary tubes, give uniform results. Melting points given by heating in capillary tubes in the usual manner are 0.5 — 2° too high and when taken rapidly ¹⁶ lead to very high values which cause confusion in the literature.

Generally the separation of homologues is best attained by fractional distillation at low pressure through efficient columns ^{14, 17} followed by crystallisation from a series of solvents; until the purity exceeds 80%, crystallisation is of little use. (Molecular distillation, which depends on the rate of evaporation rather than on the partial vapour pressure, is being increasingly used.¹⁸) In separating a substance (by crystallisation in a solvent) from an impurity with

¹⁴ J. C. Smith, *J.*, 1931, 802.

¹⁵ *J.*, 1936, 137.

¹⁶ P. A. Levene and F. A. Taylor, *J. Biol. Chem.*, 1924, **59**, 905.

¹⁷ E. Jantzen and C. Tiedcke, *J. pr. Chem.*, 1930, **127**, 277; L. Keffler and J. H. McLean, *J. Soc. Chem. Ind.*, 1935, **54**, 362 T; E. Klonk, *Z. physiol. Chem.*, 1931, **200**, 56; 1936, **242**, 250; W. Diemair and W. Schmidt, *Biochem. Z.*, 1937, **294**, 348; A. Klem, *Nature*, 1938, **142**, 616.

¹⁸ E. W. Washburn, *Bur. Stand. J. Res.*, 1929, **2**, 476; K. C. D. Hickman, *Ind. Eng. Chem.*, 1937, **29**, 968; (Miss) H. Gilchrist and (Miss) B. Karlik, *J.*, 1932, 1992.

which it forms mixed crystals it is generally advantageous to allow the solution to cool very slowly. Even then as many as ten crystallisations may be necessary in order to obtain a specimen of 99% purity and a further ten crystallisations to reach 99.9%. The best known of the higher aliphatic compounds, palmitic and stearic acids, may not yet have reached 99.9% purity, as some change in technique may show. De Visser,¹³ by crystallisation from alcohol, raised the freezing point of palmitic acid to 62.62° and of stearic acid to 69.32°; use of different solvents changed these values to 62.66° and 69.41° respectively;¹⁴ distillation, combined with twenty crystallisations from various solvents, brought the values to 62.75° and 69.62°.¹⁹

X-Ray Analysis of Films.—Interest in long-chain compounds was much stimulated by the results of X-ray investigations. It was shown^{20,21} that thin films of a homologous series of substances could yield X-ray photographs in which some of the distances (the d_1 spacings) varied linearly with the number of carbon atoms in the homologue. The lines are due to reflections from planes separating the molecules, and the methylene chain is a more or less rigid zigzag between these planes. A. Müller²² likens solid paraffins near their melting point to closely packed hexagonal pencils.

There appears to be only one type of chain, but in the earlier stages of the development of the subject other forms were considered in order to accommodate the facts that in the ethyl esters the increment of the d_1 spacing per CH_2 group was 1.22 Å. whereas in the acids it was 1.0 Å. (actually 2.0 Å. for the double molecule).²³ It was realised later that the chains could adopt various angles of tilt, but that in some esters the axis of the chain was at right angles to the end plane (a "vertical chain"). In most of the acids the chains were "tilted" and moreover the acids existed as double molecules. When the photographs of acids were compared with those of ketones in which the position of the carbonyl group was known,²⁴ the relative intensities of the orders of reflection showed that the two carboxyl groups must be together, as is now accepted for the associated forms.²⁵ Shorter spacings (d_2 and d_3) of between 4 and 5 Å., representing the breadth and thickness of the chain, remain almost constant in a homologous series.

¹⁹ J. B. Guy and J. C. Smith, unpublished result.

²⁰ A. Müller, *J.*, 1923, **123**, 2043.

²¹ S. H. Piper and E. N. Grindley, *Proc. Physical Soc.*, 1923, **35**, 269; *Ann. Reports*, 1923, **20**, 242; 1925, **22**, 254.

²² *Trans. Faraday Soc.*, 1933, **29**, 990.

²³ A. Müller and G. Shearer, *J.*, 1923, **123**, 3156.

²⁴ W. B. Saville and G. Shearer, *J.*, 1925, **127**, 591.

²⁵ N. V. Sidgwick, *Ann. Reports*, 1933, **30**, 115.

In some cases the increase of length for each CH_2 added is greater than would be expected for a methylene chain with the carbon valency angle of $109^\circ 28'$.²⁶ In the acids the longest spacing (A) shows an increase of 1.4 Å. per CH_2 group, whereas 1.22 Å. would correspond to an angle of $109^\circ 28'$.²⁷ S. H. Piper²⁸ found that ΔCH_2 corresponded to an angle of $111^\circ 46'$ in the acid salts of the fatty acids ($\text{R}\cdot\text{CO}_2\text{H}$, $\text{R}\cdot\text{CO}_2\text{K}$), and T. Malkin²⁹ calculates that the valency angle in the vertical forms of ethyl esters is 118° .

It was pointed out by L. Pauling³⁰ that rotation of long chains should be possible in the solid state. J. D. Bernal³¹ showed that in dodecyl alcohol and octadecylamine hydrochloride the molecules acquired a higher degree of symmetry with rise in the temperature and that this could be accounted for if the chain began to rotate.

A. Müller³² showed that all paraffins from $\text{C}_{21}\text{H}_{44}$ to $\text{C}_{27}\text{H}_{56}$ acquired higher (hexagonal) symmetry near the melting point, and that the rapid rise in polarisation of ketones (near the m. p.) was accompanied by a large expansion of crystal lattice.^{32a} That the chains rotate in "vertical" transparent crystal forms is now a widely accepted view³³ and explains the similarity of these crystals to liquid crystals, as is pointed out in the section on Binary Systems.

Obviously the method of measuring the spacings in films has yielded very valuable results, but many outstanding problems can be solved only by detailed analysis of single crystals,³⁴ as has been done with the dibasic acids,³⁵ nonacosane,³⁶ triacontane³⁷ and cetyl palmitate.³⁸ Work on unimolecular films on liquid and solid surfaces has been reviewed by N. K. Adam.³⁹ X-Ray analysis of liquid paraffins has shown that the chains are roughly parallel even in the liquid state.⁴⁰ The diffraction of electrons by long-chain

²⁶ *Ann. Reports*, 1931, **28**, 384.

²⁷ S. H. Piper, T. Malkin, and H. E. Austin, *J.*, 1926, 2310.

²⁸ *J.*, 1929, 234.

²⁹ *J.*, 1931, 2796.

³⁰ *Physical Rev.*, 1930, **36**, 430.

³¹ *Nature*, 1932, **129**, 870; *Z. Krist.*, 1932, **83**, 153.

³² *Nature*, 1932, **129**, 436; *Proc. Roy. Soc.*, 1932, *A*, **138**, 514.

^{32a} *Proc. Roy. Soc.*, 1938, *A*, **166**, 316.

³³ *Ann. Reports*, 1937, **34**, 184; T. Malkin, *J.*, 1935, 726; W. O. Baker and C. P. Smyth, *J. Amer. Chem. Soc.*, 1938, **60**, 1229.

³⁴ *Ann. Reports*, 1935, **32**, 227.

³⁵ W. A. Caspari, *J.*, 1928, 3235; 1929, 2709.

³⁶ A. Müller, *Proc. Roy. Soc.*, 1928, *A*, **120**, 437.

³⁷ R. Kohlhaas and K. H. Soremba, *Z. Krist.*, 1938, **100**, 47.

³⁸ R. Kohlhaas, *ibid.*, 1938, **98**, 418.

³⁹ "The Physics and Chemistry of Surfaces," 2nd Edn., Oxford, 1938.

⁴⁰ G. W. Stewart, *Physical Rev.*, 1928, **31**, 174; B. E. Warren, *ibid.*, 1933, **44**, 969.

compounds has yielded results in excellent agreement with those from X-ray studies.⁴¹

Polymorphism.—Crystal analysis with the help of X-ray measurements, by detecting different cell dimensions for compounds under varying conditions, has not only indicated polymorphism but has in some cases given an explanation of the phenomenon.

Previous to 1920 only a few higher aliphatic compounds were known in more than one crystalline form, examples being the glycerides, oleic acid and cetyl acetate, but it is now recognised that the majority of long-chain compounds are polymorphous. The more systematic aspects of polymorphism in the fatty acids,^{42, 89, 27, 43} paraffins,⁴⁴ alcohols,⁴⁵ and dicarboxylic acids³⁵ were emphasised by the X-ray studies; *isobutyl* palmitate and stearate were visibly dimorphous.⁴⁶ Hexadecane, ethyl palmitate and ethyl stearate were handled for some years without recognition of their polymorphism, although there was some confusion over the difference between the X-ray spacings of "melted" and of "pressed" films. When the polymorphism of these esters was pointed out,^{14, 47} it was obvious that "melted" films were composed of the metastable, transparent forms and that pressing with a spatula would hasten the change to the stable, opaque forms. Moreover, in mixtures of esters the transparent forms were stabilised,¹⁴ yielding longer spacings than either of the pure components.²⁹

Examination of binary systems of homologues produced some of the conditions under which metastable forms were detectable, so that hexadecane, octadecane and cetyl iodide were seen to be dimorphous.⁴⁸ Adopting the binary system technique, J. W. C. Phillips and S. A. Mumford^{49, 54, 55, 56} made an extended study of polymorphism. Cooling curves have been used by Phillips and Mumford,⁴⁹ Malkin,²⁹ and (Miss) J. D. Meyer and E. E. Reid,⁵⁰ optical methods by D. Vorländer and W. Selke⁴⁶ and by C. Weygand and W. Grüntzig.⁵¹

Carboxylic acids. W. E. Garner and F. C. Randall⁸⁹ noticed that, when nonoic and undecoic acids were cooled about 20° below

⁴¹ P. A. Thiessen and T. Schoon, *Z. physikal. Chem.*, 1937, **36**, B, 216.

⁴² A. Gascard, *Ann. Chim.*, 1921, **15**, 332.

⁴³ G. M. de Boer, *Nature*, 1927, **119**, 634; S. H. Piper, *Trans. Faraday Soc.*, 1929, **25**, 348.

⁴⁴ A. Müller and W. B. Saville, *J.*, 1925, **127**, 599.

⁴⁵ T. Malkin, *J. Amer. Chem. Soc.*, 1930, **52**, 3739.

⁴⁶ D. Vorländer and W. Selke, *Z. physikal. Chem.*, 1927, **129**, 435.

⁴⁷ J. W. C. Phillips and S. A. Mumford, *J.*, 1931, 1732.

⁴⁸ J. C. Smith, *J.*, 1932, 737.

⁴⁹ *J.*, 1932, 898.

⁵⁰ *J. Amer. Chem. Soc.*, 1933, **55**, 1574.

⁵¹ *Z. anorg. Chem.*, 1932, **206**, 304, 313.

the freezing points, they changed enantiotropically into opaque forms; in general, two forms are visibly detectable for "odd" acids from C_9 to C_{25} , whereas "even" acids appear to be of one type. X-Ray analysis, however, shows the existence of three forms (A, B, and C spacings) for "even" acids and of four forms (A', B', C' and D' spacings) for "odd" acids.⁴³ Forms with A (and A') spacings seem the least easily obtained and have a vertical chain; they are said to occur in palmitic and stearic acids only when these are fairly pure,²⁷ and only in mixtures when the chain length is 23 to 27 carbon atoms.⁵² The solvent used for crystallising the acid⁵³ and the temperature to which the film is heated have a big effect on the spacings obtained. Films of "even" acids (lauric to stearic) which show A and B spacings will on heating near the m. p. show only C spacings.⁴³ As the history of the specimen does not appear to affect the m. p. of an acid, it must be assumed that the same form is always present at the melting point. The acid sodium or potassium salts ($R\cdot CO_2H, R\cdot CO_2Na$) yield only an A spacing, so their identification by X-rays is simple.²⁸

Methyl esters. Only a tilted form with double molecules has so far been observed for the methyl esters of even acids. Methyl esters of odd acids crystallise either in double molecules with an angle of tilt of 67.5° or in single molecules with 75° tilt,^{29, 54} but the position is not quite clear, as it is found that the heats of transition and crystallisation of methyl nonadecoate are practically identical with those of ethyl nonadecoate where both forms are of single molecules.⁹⁷

Ethyl esters. At least three kinds of polymorphism are observed^{54, 47, 55, 56, 14, 57, 49, 58}: (i) for esters up to ethyl myristate the opaque β -forms of both even and odd members are stable and the transparent α -forms are metastable (monotropic polymorphism); (ii) from ethyl myristate to ethyl eicosanoate α -forms of the odd members are stable near the melting point and change enantiotropically to the β -forms on cooling; α -forms of the even members are metastable (except in mixtures) and change monotropically to the β -forms; (iii) above ethyl eicosanoate the α -forms of both

⁵² S. H. Piper, A. C. Chibnall, and E. F. Williams, *Biochem. J.*, 1936, **30**, 100, 112.

⁵³ F. Francis, F. J. E. Collins, and S. H. Piper, *Proc. Roy. Soc.*, 1937, **A**, **158**, 691; *Ann Reports*, 1937, **34**, 183.

⁵⁴ J. W. C. Phillips and S. A. Mumford, *J.*, 1934, 1657.

⁵⁵ *Idem*, *J.*, 1932, 898.

⁵⁶ *Idem*, *Rec. Trav. chim.*, 1933, **52**, 175, 181.

⁵⁷ (Miss) P. C. Carey and J. C. Smith, *J.*, 1933, 635.

⁵⁸ S. H. Piper, A. C. Chibnall, and E. F. Williams, *Biochem. J.*, 1934, **28**, 2175.

odd and even members are stable near the melting point (monotropic polymorphism). These complications are partly due to the intersection of the melting point curves (m. p. plotted against number of carbon atoms); the α -m. p. curve (both "even" and "odd") begins below the β -curves, but, rising more steeply, intersects the β - "odd" curve near ethyl pentadecoate and the β - "even" curve near ethyl eicosanoate.⁵⁴ All the α -(transparent) forms have vertical chains and the m. p.'s fit on a smooth curve.²⁹ There is some evidence for the existence of lower-melting γ -forms.⁵⁶ The melting point of ethyl hexatetracontanoate ($C_{45}H_{91}\cdot CO_2Et$), 90.5° , is higher than that expected by extrapolation of the α -m. p. curve, and a β -form is suggested.⁵³

n-Propyl, *n*-butyl and *n*-amyl esters of higher fatty acids have been much less fully investigated.^{59, 60, 46, 61}

Alcohols. The melting-point curve (m. p. against no. of C atoms) for the α -forms intersects the β -m. p. curve at C_{13} . For dodecyl alcohol the transparent α -form changes monotropically to the opaque β -form. Tetradecyl alcohol, like the higher members of the series, solidifies in the α -form and changes enantiotropically to the β -form on further cooling.⁵⁴ All the alcohols above dodecyl are in the α -form at the m. p.'s,⁴⁵ which are sometimes unsharp because of the transitions taking place in the solid; the α -forms have vertical chains (rotating),³¹ For the "even" members the β -forms have tilted chains; the "odd" β -forms are opaque but they are not tilted. It has been shown that they are vertical, non-rotating forms.^{62, 63}

Acetates and formates. The polymorphism of the "even" acetates is very similar to that of ethyl esters with the same number of carbon atoms.⁵⁴ Heptadecyl acetate readily yields a γ -form.^{57, 64} Cetyl formate exists in transparent and opaque forms.¹²

Halides. These have not been fully investigated. Cetyl iodide is dimorphous;⁴⁸ the "even" iodides from C_{22} to C_{30} have α - and β -forms; C_{32} , C_{34} , C_{36} iodides have so far given only α -forms.^{53, 29} Cetyl chloride (but not cetyl bromide) is dimorphous.⁴⁷

Paraffins. For "even" paraffins there are transparent vertical forms with rotating chains and also opaque tilted forms. With pure hexadecane the transparent form has not been obtained, but addition of 1% of octadecane causes this form to crystallise on cooling and then change suddenly to the opaque crystals; addition of more octadecane stabilises the transparent form. Similarly the transparent crystals of octadecane are not obtained from the pure sub-

⁵⁹ N. K. Adam, *Proc. Roy. Soc.*, 1922, A, **101**, 516.

⁶⁰ G. S. Whitby, *J.*, 1926, 1458.

⁶¹ T. Malkin, *Trans. Faraday Soc.*, 1933, **29**, 977.

⁶² D. A. Wilson and E. Ott, *J. Chem. Physics*, 1934, **2**, 231.

⁶³ T. Malkin, *J.*, 1935, 726.

stance.⁴⁸ Above octadecane the polymorphism becomes enantiotropic and the transparent form is stable near the melting point. From hexacosane onwards the paraffins can exist in a third modification with a more highly tilted chain.⁹ The existence of these types of polymorphism explains the contrast between petroleum jelly and paraffin wax. "Odd" paraffins above undecane, on cooling, crystallise in transparent, vertical, rotating forms, which on further cooling change into opaque, vertical, non-rotating forms, and the reverse changes occur on heating. The "odd" paraffins do not crystallise with tilted chains.^{9, 44, 64, 65}

In general (and with the possible exception of the acids) a longer chain, a higher temperature, an odd number of carbon atoms, or the presence of impurity favours crystallisation in vertical forms.

Binary Systems.—The collection of binary systems on pp. 261—262 illustrates many of the types predicted⁶⁶ for substances which form solid solutions. Roozeboom's Type II, a continuous series of solid solutions with a maximum, is absent, but it is rarely found in organic systems (examples are *d*- and *l*-carvoxime,⁶⁷ *n*-propyl and *n*-butyl gallate⁶⁸). The narrow range of temperatures covered by each of these systems, compared with systems of inorganic compounds, and the low heat conductivity of the substances make the determination of solidus points difficult, and it is doubtful whether equilibrium is established between solid and liquid phases.⁶⁹

The systems on p. 261 are mainly those of the α -forms of the substances, transparent crystals with rotating chains.³¹ D. Vorländer⁷⁰ has pointed out from the study of the optical properties the similarity between liquid crystals and the transparent forms of long-chain compounds in that both possess freedom of movement round a long axis. In discussing isomorphism among liquid crystals, he quotes two binary systems, *p*-azoxyanisole-*p*-azoxyphenetole (Fig. XIV) and *p*-azoxyanisole-*p*-methoxycinnamic acid (Fig. XV).⁷¹ Both pairs, in the equilibrium between the liquid crystal and the solid, give a eutectic and show no mixed crystal formation.

⁶⁴ (Miss) P. C. Carey and J. C. Smith, *J.*, 1933, 1348.

⁶⁵ A. Müller, *Proc. Roy. Soc.*, 1928, *A*, **120**, 437; 1930, *A*, **127**, 417; 1932, *A*, **138**, 514.

⁶⁶ H. W. B. Roozeboom, *Z. physikal. Chem.*, 1899, **30**, 385.

⁶⁷ J. H. Adriani, *ibid.*, 1900, **33**, 469.

⁶⁸ R. M. Harris and J. C. Smith, *J.*, 1935, 1220.

⁶⁹ E. Jantzen, *Z. angew. Chem.*, 1931, **44**, 482; W. Brüll, *Naturwiss.*, 1934, **22**, 436.

⁷⁰ *Z. Krist.*, 1931, **79**, 61; D. Vorländer with K. Ost, *Ber.*, 1938, **71**, 1688. See also T. Malkin.⁶¹

⁷¹ A. Prins, *Z. physikal. Chem.*, 1909, **67**, 689; A. C. de Koch, *ibid.*, 1904, **48**, 129.

For the equilibrium, liquid crystal-amorphous liquid, both pairs form a continuous series of mixed crystals. Thus in the liquid crystal form in each case the molecules possess a higher degree of symmetry. The first pair very readily form mixed (liquid) crystals; the second pair, as would be expected from their differing structures, form mixed crystals rather less readily, the liquidus curve showing a minimum. The higher aliphatic binary systems now provide a confirmation of Vorländer's views.

Crystals of ethyl palmitate and ethyl stearate are sufficiently similar in the opaque (β) form to yield mixed crystals, a discontinuous series with a eutectic (Fig. VII); in the α -form the crystals are so similar that they yield an unbroken series of mixed crystals without a minimum. Mixtures of "odd-even" esters (Fig. VIII) show the closest conformation possible, the mixed melting-point curve being a straight line. As the carbon chain of the ester becomes shorter, the ability to assume the α -form decreases until at ethyl decoate apparently only the β -form (Figs. IX, X, XI) exists. It seems in Fig. I that the β -forms of the paraffins are tending towards a eutectic, while the α -forms (rotating chains) give a continuous series of solid solutions; rather surprisingly the (α -) paraffins seem to form solid solutions less readily than do the (α -)ethyl esters, as is shown by the minimum in the curve (Fig. I). The higher members, however, give straight line mixed melting-point curves (Fig. III).

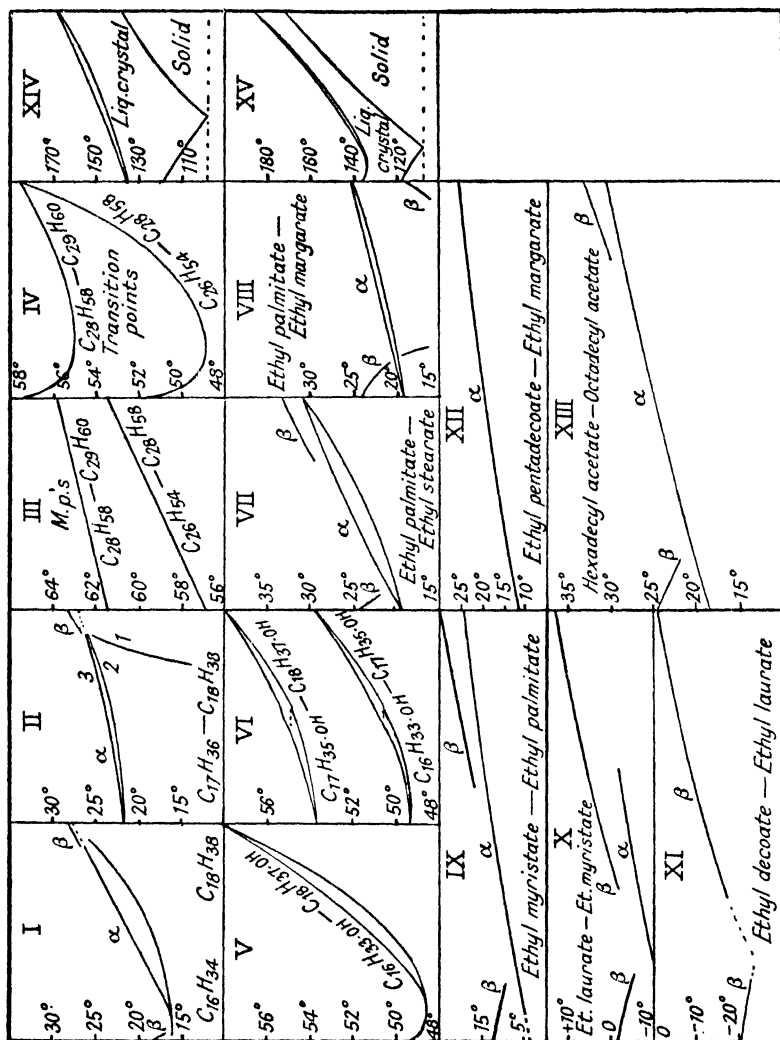
The β -forms of the paraffins give larger depressions of melting point and this part of the system can be followed as a transition temperature in the solid phase (Figs. II 1, IV). Chibnall and his collaborators⁹ have used these transition temperatures in the analysis of paraffins from plant waxes. For example, an equimolecular mixture of $C_{29}H_{60}$ and $C_{31}H_{64}$ has a sharp melting point (65.6°) at almost the same temperature as that of pure $C_{30}H_{62}$ (65.7°), but the transition temperatures show the difference between the pure hydrocarbon and the mixture.

In the "even" alcohols the α -forms are stable at the melting point, and the curve shows moderate ease of mixed crystal formation (Fig. V), while in the "even-odd" alcohol systems there is a discontinuity (Fig. VI). This discontinuity shows that there is persistence of one crystal lattice up to 50 molecules % and then a sudden change to the lattice of the other component (compare the systems, cadmium-mercury and cadmium-magnesium⁷²). If in the "odd" alcohols also the α -form is stable at the melting point, the reason for this abrupt change is not obvious.

It is interesting to compare these aliphatic systems with those of pairs of the bromides of phosphorus, arsenic, antimony and

⁷² "International Critical Tables," Vol. II, p. 429.

bismuth,⁷³ those of the diphenylene oxides, sulphides and selenides, dioxides, disulphides and diselenides,⁷⁴ and the aromatic systems : ⁷⁵



the more similar the components of a system, the more readily are mixed crystals formed.

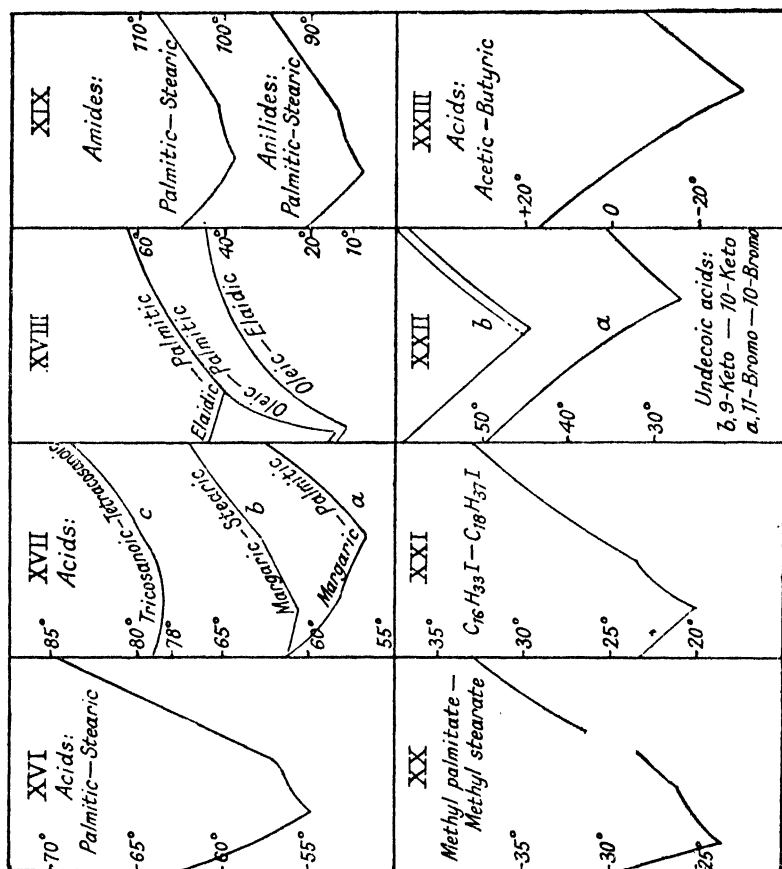
Most of the binary systems on p. 262 show a eutectic, which

⁷³ N. A. Pušin and J. Makuc, *Z. anorg. Chem.*, 1938, **237**, 177.

⁷⁴ N. M. Cullinane and C. A. J. Plummer, *J.*, 1938, 63.

⁷⁵ H. G. Grimm, M. Günther, and H. Tittus, *Z. physikal. Chem.*, 1931, **B**, **14**, 169.

indicates that solid solutions are formed with some difficulty. In the acids (Figs. XVI, XVIIa and b) the forms stable at the melting point have tilted chains, while with tricosanoic and tetracosanoic acids (Fig. XVIIc) at least some of the mixtures crystallise with a vertical chain (A spacing).⁵² If these A forms really are stable



at the melting point, this system also shows the greater ease with which vertical forms yield solid solutions. The systems oleic-palmitic, elaidic-palmitic and oleic-elaidic acids (Fig. XVIII) are made up almost entirely of the crystals from the higher-melting component in each case; these crystals are opaque and probably have a tilted chain. The X-ray data for the unsaturated acids are in need of revision.²³

In the two substituted undecanoic acid systems (Fig. XXII) different positions of the substituent as well as a shorter chain length bring

about a larger depression in melting point, and the depressions with acetic and butyric acids (Fig. XXIII) are of the order expected for components which do not form solid solutions. Amides, anilides (Fig. XIX), methyl esters and iodides (Figs. XX and XXI) are also systems of opaque forms. The other point of interest is their bearing on the question of compound formation.

- I.⁴⁸ For $C_{16}H_{34}-C_{16}H_{32}$, see ref. (76).
- II. 1, transition $\alpha \longrightarrow \beta$; 2, solidus; 3, liquidus. $C_{17}H_{36}-C_{16}H_{34}$ is very similar.⁶⁴
- III.⁹ IV. Transition points $\alpha \longrightarrow \beta$ of the paraffin in III.⁹
- V.¹⁴ For systems of alcohols C_{26} to C_{34} , see Chibnall.⁵⁸
- VI.⁶⁴ VII.¹⁴ VIII.^{57, 56} IX.⁵⁶ X.⁵⁶ XI.⁵⁶ XII.⁵⁶
- XIII.⁵⁴ For dodecyl-tetradecyl and tetradecyl-hexadecyl acetates, see ref. 54.
- XIV. *p*-Azoxyanisole-*p*-azoxyphenetole.^{70, 71}
- XV. *p*-Azoxyanisole-*p*-methoxycinnamic acid.^{70, 71}
- XVI.^{13, 53, 79} Other "even-even" acid] systems,^{77, 78} Chibnall and collaborators.^{52, 58}
- XVII. "Odd-even" acids: (a) margaric-palmitic, (b) margaric-stearic;⁷⁹ (c) tricosanoic-tetracosanoic.^{6, 79, 52} For other "odd-even" systems, see ref. 52.
- XVIII. Oleic acid-elaidic acid;⁸⁰ oleic-palmitic;⁸¹ elaidic-palmitic (J. C. Smith, unpublished).
- XIX. (J. B. Guy and J. C. Smith, unpublished). XX. (*idem*, *ibid.*). XXI.⁴⁸ XXII a;⁸² b.⁸³ XXIII.⁷⁸

Compound Formation.—Mixtures of "even" acids from dodecoic to eicosanoic give melting-point curves similar to that in Fig. XVI; formation of a compound with a non-congruent melting point is generally inferred. Few "even-odd" systems have been investigated with pure acids, but they seem to indicate less stable and not necessarily 1:1 compounds (Fig. XVIIa, b, and perhaps c). This behaviour of carboxylic acids would be expected, since they exist as double molecules in solution⁸⁴ and, for the lower members, at

⁷⁶ S. L. Langedijk and W. C. B. Smithuysen, *Rec. Trav. chim.*, 1938, **57**, 1050.

⁷⁷ G. T. Morgan and A. R. Bowen, *J. Soc. Chem. Ind.*, 1924, **43**, 346 r.

⁷⁸ L. A. Bhatt and H. E. Watson, *J. Indian Inst. Sci.*, 1930, **13**, A, 141.

⁷⁹ J. C. Smith, *J.*, 1936, 625.

⁸⁰ H. N. Griffiths and T. P. Hilditch, *J.*, 1932, 2315.

⁸¹ A. Lapworth, (Mrs.) L. K. Pearson, and E. N. Mottram, *Biochem. J.*, 1925, **19**, 7; J. C. Smith, unpublished results.

⁸² P. L. Harris and J. C. Smith, *J.*, 1935, 1108.

⁸³ (Miss) M. L. Sherrill and J. C. Smith, *J.*, 1937, 1501.

⁸⁴ P. W. Robertson, *J.*, 1903, **83**, 1425; H. N. Brocklesby, *Canadian J. Res.*, 1936, **14**, B, 222; C. R. Bury and H. O. Jenkins, *J.*, 1934, 688; M. Trautz and W. Moschel, *Z. anorg. Chem.*, 1926, **155**, 13.

temperatures above the boiling point; ⁸⁵ a ring formula is generally accepted.²⁵ If acids X and Y exist as X-X and Y-Y units, some X-Y units should occur in a mixture, and similarly the amides and anilides should yield equimolecular compounds.

The unsaturated acid system, oleic-elaidic, and the unsaturated-saturated system, oleic-palmitic, give no sign of compound formation (Fig. XVIII) (elaidic-palmitic is a doubtful case), nor do the systems in Figs. XXII and XXIII. Methyl ester and alkyl iodide systems (Figs. XX and XXI) show "compounds" with non-congruent melting points.

X-Ray spacings show that the saturated and the unsaturated acids crystallise in double molecules;²³ methyl (but not ethyl) esters,²⁹ methyl (but not ethyl) ketones,²⁴ alkyl iodides²⁹ and alcohols^{45, 62} form double molecules. That is, the "reactive" ends come together in the middle and the pattern repeats itself after each two molecules. In solution, molecular-weight determinations show that the saturated acids are mainly in double molecules and that unsaturated acids are less associated.⁸⁴ The presence of impurities can obliterate the changes in a liquidus curve which indicate the compounds between acids.^{14, 79} Lack of symmetry may conceivably prevent crystallisation of a compound between a saturated and an unsaturated acid, but on the other hand it may be the demands of symmetry (or the ease of packing) which cause methyl esters to crystallise in double molecules. The position is not clear and attempts to solve this aliphatic and other similar problems by X-ray methods^{27, 37} and by measurement of dielectric constant^{86, 87} or of fluidity⁸⁸ have met with little success.

Thermal Investigations.—Heats of crystallisation, transition temperatures, and specific heats of several series of long-chain compounds have been systematically examined.⁸⁹⁻⁹⁸

⁸⁵ (Miss) T. M. Fenton and W. E. Garner, *J.*, 1930, 694; V. C. E. Burnop, *J.*, 1938, 1614.

⁸⁶ E. Eisenlohr and G. Meier, *Ber.*, 1938, **71**, 1005.

⁸⁷ K. Hrynakowski and J. Jesko, *ibid.*, p. 1415.

⁸⁸ R. H. Ewell, *J. Chem. Physics*, 1937, **5**, 967.

⁸⁹ W. E. Garner and F. C. Randall, *J.*, 1924, **125**, 881.

⁹⁰ W. E. Garner, F. C. Madden, and J. E. Rushbrooke, *J.*, 1926, 2491.

⁹¹ W. E. Garner and J. E. Rushbrooke, *J.*, 1927, 1351.

⁹² W. E. Garner and (Miss) A. M. King, *J.*, 1929, 1849.

⁹³ (Miss) A. M. King and W. E. Garner, *J.*, 1931, 578.

⁹⁴ W. E. Garner, (Miss) K. Van Bibber, and (Miss) A. M. King, *J.*, 1931, 1533.

⁹⁵ (Miss) A. M. King and W. E. Garner, *J.*, 1934, 1449 (summarising paper).

⁹⁶ *Idem*, *J.*, 1936, 1368 (summarising paper).

⁹⁷ *Idem*, *ibid.*, p. 1372.

⁹⁸ G. S. Parks and H. M. Huffman, *Ind. Eng. Chem.*, 1931, **23**, 1138; H. M. Huffman, G. S. Parks, and M. Barmore, *J. Amer. Chem. Soc.*, 1931, **53**, 3876; G. S. Parks, H. M. Huffman, and S. B. Thomas, *ibid.*, 1930, **52**, 1032.

In any homologous series where similar crystal forms are stable at the melting point the heat of crystallisation per CH_2 group is constant. Where the crystal form alternates, as in the "odd" and "even" members of the fatty acids, the heat of crystallisation alternates and has its minimum at about the same point in the series as does the melting point.^{89, 90, 98} The heat of crystallisation (Q) of even-number fatty acids (above C_{10}), plotted against the number of carbon atoms (n), gives a straight line, as also does Q/T , where $T = \text{m. p. in degrees absolute}$:

$$Q = 1.030n - 3.61; \quad Q/T = 0.002652n - 0.0043$$

Hence
$$T = (1.030n - 3.61)/(0.002652n - 0.0043)$$

This equation for T predicts a maximum (the convergence temperature) of 115°C. for the series.⁹⁰ Similar equations are derived for the odd acids,⁹² the ethyl^{95, 54} and methyl⁹⁷ esters, and the paraffins.⁹⁴ [E. B. Moullin⁹⁹ finds that, for paraffins of n carbon atoms, $\log(n - 2)$, plotted against melting point, gives a straight line from $n = 27$ to $n = 8$ and probably lower. The analogy between an acid and a paraffin of double the number of carbon atoms is pointed out.]

Defining the melting point as the temperature at which the probability of detachment of a molecule from a surface is equal to the probability of its attachment, Garner and his pupils develop a theory of melting from the X-ray model of the crystal. On the surface the molecule will be attached by $\frac{1}{2}(n - 2)\text{CH}_2$ groups and by the two end groups; in melting, a molecule will leave the surface in stages in which one point of attachment may be broken at a time and equations are derived in terms of energies of activation.^{90, 96} This probability factor is held responsible⁹³ for the minimum in the melting points of homologous series between C_3 and C_5 (the theory does not deal specifically with the transparent forms in which the chains are rotating below the melting point).

Besides the probability factor an important contribution to melting in the case of the lower members must be made by the end groups. The heat of crystallisation of each CH_2 group for the acids above decolic is 1.030 kg.-cals. and from this the heat of crystallisation of the end groups is calculated⁹⁰ to be -1.55 kg.-cals. All homologous series give negative values (from -0.53 to -3.90 kg.-cals.) for the two terminal groups in members with more than ten carbon

⁹⁹ *Proc. Camb. Phil. Soc.*, 1938, **34**, 459. For other formulæ for calculating m. p.'s in homologous series, see also J. B. Austin, *J. Amer. Chem. Soc.*, 1930, **52**, 1049; V. K. Nikiforov and I. I. Korolkov, *J. Gen. Chem. Russia*, 1937, **7**, 2139; R. Kobuyashi, *J. Soc. Chem. Ind. Japan*, 1937, **40**, 341 B; C. D. Nenizescu, S. Titeica, and I. Irimescu, *Naturwiss.*, 1938, **26**, 629.

atoms.⁹⁶ From the area of cross section of the crystal cell it seems that the end groups, whatever their nature, are in an "expanded" state and can move about much more freely than the rest of the chain; on *melting*, the end groups approach more closely and give a positive heat value.⁹¹ For the lower members (perhaps C_6 upwards) this negative heat of crystallisation lowers the melting point, but its effect is felt less and less as the methylene chain becomes longer. In all series there is a convergence temperature of about 120° as the methylene chain becomes the dominant factor.^{91, 96} As regards the first members of a series there are many disturbing factors, especially from the terminal groups. If it is assumed that the heat of crystallisation of the CH_2 group is constant right down the series, then the heat of crystallisation of the end groups changes from negative to positive: ⁹⁰

C_2 C_4 C_6 C_8 C_{10} C_{12} C_{14} C_{16} C_{20}
 +2.77 +0.58 -0.52 -1.07 -1.55 -1.55 -1.62 -1.44 -1.59 kg.-cals.

The value for acetic acid (+2.77 cals.) is greater than the total heat of crystallisation of butyric acid (+2.62), although butyric acid has two CH_2 groups.⁹⁶ When one end grouping is very polar, as in the acids, the amides or the alcohols, the degree of association must have a large effect on the heat of crystallisation. According to Garner and Rushbrooke⁹¹ the main cause of the very high melting points of the lower amides is the exceptionally high heat of crystallisation of the $(-CO\cdot NH_2)_2$ group in the associated compound. Crystalline form should have a big effect on the melting point, and X-ray studies on the acids from formic to decoic show irregular spacings up to hexoic acid.^{99a}

The thermal investigations divide crystals of long-chain substances very sharply into those with vertical and those with tilted chains. Vertical forms have a low heat of crystallisation, a high specific heat, a large cross-section, and a large coefficient of expansion,^{94, 95, 96} indicating that the molecules possess relatively great mobility (as would be expected with a rotating chain).

In the tilted forms, although the angle of tilt varies considerably from series to series, the variation in the heat of crystallisation per CH_2 group in the different series is relatively small. The specific heat of the solid in equilibrium with the liquid is normal, *i.e.*, it is less than that of the liquid. These data are summarised: ^{94, 95, 96}

Form.	Heat of crystn. per CH_2 , kg.-cals.	Specific heat of solid form.	Area of cross section, \AA^2 .
Vertical	0.61 — 0.84	0.63 — 1.05	19.9
Tilted	0.97 — 1.08	0.43 — 0.48	18.4

$\alpha \longrightarrow \beta$ Transitions of "odd" acids are regarded as an example

^{99a} R. E. Gibbs, *J.*, 1924, **125**, 2622.

of unilateral transition in the solid state^{92, 1} exemplified by the simultaneous occurrence of three spacings (corresponding to three crystal forms) on the same photograph of an "odd" acid.⁴³ The heats of transition $\alpha \rightarrow \beta$ for hydrocarbons are approximately four times as great as those for the fatty acids.⁹⁴ For the hydrocarbons it is a change from rotating to non-rotating forms, followed in the "even" hydrocarbons by a tilt of the molecule; for acids, usually only a change of tilt is incurred.

A. R. Ubbelohde² has determined specific heats of paraffins and observed marked pre-melting. K. H. Meyer and A. van der Wyk³ discuss the effect of the heat of fusion on the solubility of paraffins.

Alternation in Melting Point.—This is a subject which has attracted the attention of most chemists who have worked with homologous compounds. All homologous series show alternation in melting point between "even" and "odd" members early in the series: the alcohols after amyl alcohol show only slight alternation, a gentle zigzag when the melting points are plotted against the number of carbon atoms; the paraffins zigzag more decidedly as far as $C_{20}H_{42}$; for the acids, alternation persists so that the melting point of $C_{21}H_{42}O_2$ is just equal to that of $C_{20}H_{40}O_2$. The dicarboxylic acids provide an extreme case, the melting points of odd and even members falling on two converging curves. Alkyl iodides²⁹ and bromides⁵⁰ are unusual, for in both cases the melting point curve of the "odd" lies above that of the "even" members.

Several theories have been put forward to explain this alternation and a bibliography is given by T. Malkin.²⁹ G. Tammann,⁴ working with the lower fatty acids, ascribed alternation to the existence of polymorphism in the even members, though the evidence was scanty. W. E. Garner and F. C. Randall⁸⁹ decided from the heats of crystallisation of odd and even acids that alternation was due to "a difference in crystalline structure". W. A. Caspari³⁵ analysed well-developed crystals of the dicarboxylic acids and found that the even-number acids crystallised with two molecules and the "odd" acids with four molecules in the unit cell, as should be required by the symmetry in the two cases. He inferred that "this difference in crystal structure cannot be unconnected with the alternation in melting point."

T. Malkin²⁹ noted that when the melting points of the transparent forms of ethyl esters were plotted there was no alternation, and similarly with transparent forms of hydrocarbons, methyl ketones,

¹ E. Baur, *Z. physikal. Chem.*, 1928, **137**, 63.

² *Trans. Faraday Soc.*, 1938, **34**, 282, 292.

³ *Helv. Chim. Acta*, 1937, **20**, 1313.

⁴ *Z. anorg. Chem.*, 1920, **109**, 221.

and alcohols (compare C. Weygand and W. Grünzig on the glycerides ⁵¹); the opaque forms of the esters, however, showed decided alternation. Malkin infers that alternation is a property of crystals with tilted chains. He shows diagrammatically ^{29, 61} how "even" tilted chains may be separated by closely packed planes, all similar, whereas "odd" tilted chains should be separated by planes alternately loosely and closely packed. The loose packing in "odd" chains is thought to cause easier separation and so lower melting. This theory, which has been extended to the glycerides, ⁵ has been vehemently criticised by P. E. Verkade and J. Coops, ⁶ one of their objections being that alkylmalonic acids, although crystallising with vertical chains, yet show alternation in melting point. Obviously these are cases where the measuring of long spacings will not give the necessary information and detailed crystal analysis is urgently required.

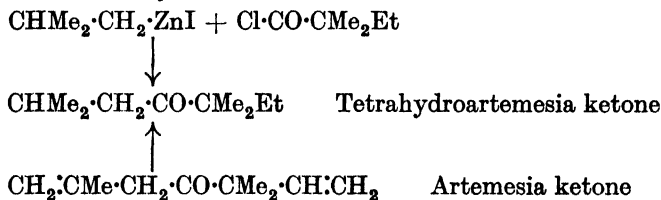
The alternation of various properties of the *liquid* state reported by O. Biach ⁷ has been disproved by more exact measurements: alternation is confined to properties of the crystalline state. ⁸

J. C. S.

5. TERPENES.

Monoterpenes.

Syntheses.—The structure shown below for Artemesia ketone was advanced by Y. Asahina and E. Yoshitomi ¹ and Y. Asahina and S. Takagi ² from a study of the oxidation products of the ketone and those of its tetrahydro-derivative; it showed an abnormal arrangement of the isoprene residues and was therefore open to criticism. ³ The structure, however, has now been established by the synthesis of the tetrahydro-ketone from $\alpha\alpha$ -dimethylbutyryl chloride and isobutylzinc iodide: ⁴



⁵ C. E. Clarkson and T. Malkin, *J.*, 1934, 666; *Ann. Reports*, 1934, **31**, 159; T. Malkin and Riad el Shurbagy, *J.*, 1936, 1628; *Ann. Reports*, 1936, **33**, 220.

⁶ *Rec. Trav. chim.*, 1933, **52**, 747.

⁷ *Z. physikal. Chem.*, 1905, **50**, 43.

⁸ P. E. Verkade, J. Coops, and H. Hartman, *Rec. Trav. chim.*, 1926, **45**, 585.

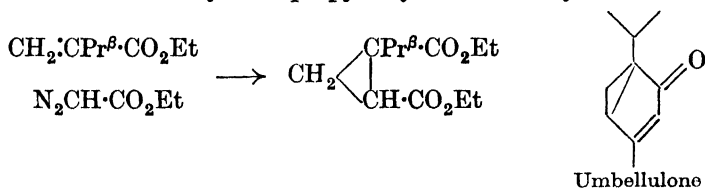
¹ *J. Pharm. Soc. Japan*, 1917, **424**, 1.

² *Ibid.*, 1920, **464**, 837.

³ J. L. Simonsen, "The Terpenes," I, 90.

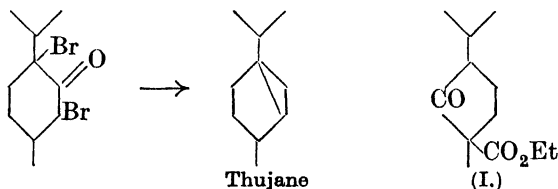
⁴ L. Ruzicka, T. Reichstein, and R. Pulver, *Helv. Chim. Acta*, 1936, **19**, 646.

Some interesting syntheses have been performed in the thujane, carane and pinane series. S. K. Ranganathan and E. O. Phillips,⁵ and G. R. Ramage and J. L. Simonsen⁶ simultaneously synthesised *cis*- and *trans*-1-isopropylcyclopropane-1:2-dicarboxylic acid by the condensation of ethyl α -isopropylacrylate with ethyl diazoacetate:⁷



The same acids have been obtained by H. N. Rydon⁸ from ethyl isopropylfumarate and diazomethane. The *cis*-acid was resolved by Ranganathan and by Rydon and the *l*-form was shown to be identical with umbellularic acid, obtained by the degradation of umbellulone.⁹

P. C. Guha and B. Nath¹⁰ have shown that 2:4-dibromomenthone, obtained by the bromination of *l*-menthone in chloroform solution, yields thujane when it is reduced by the Clemmensen method.



P. C. Guha and S. Krishnamurthy¹¹ have converted (I) into the corresponding cyclopentene derivative by reduction and dehydration and then into the bicyclo[0:1:3]hexane derivative with the aid of diazomethane; after having been hydrolysed and decarboxylated, the last product yielded thujane.

Carane has been similarly synthesised¹² from ethyl 1-methyl- Δ^3 -cyclohexene-4-carboxylate.

Syntheses of verbanone, δ -pinene and pinane have been carried out by G. Komppa and A. Klami.¹³ Methyl pinononate was converted by the Reformatsky reaction, dehydration, hydrolysis and reduction successively into (II). The destructive distillation of the

⁵ *J. Indian Chem. Soc.*, 1936, **13**, 419.

⁶ *J.*, 1936, 828.

⁷ Cf. K. von Auwers and F. König, *Annalen*, 1932, **496**, 27, 252; J. Owen and J. L. Simonsen, *J.*, 1933, 1225.

⁸ *J.*, 1936, 829.

⁹ F. Tutin, *J.*, 1906, **89**, 1104.

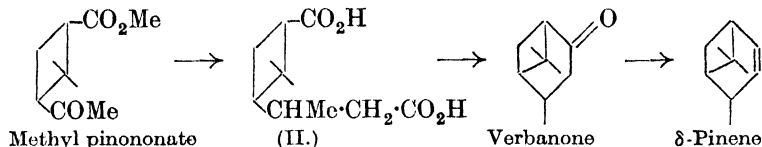
¹⁰ *Ber.*, 1937, **70**, 931.

¹¹ *Ibid.*, p. 2112.

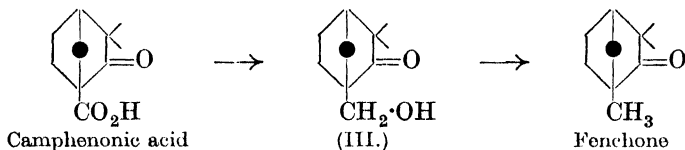
¹² P. C. Guha and D. K. Sankaran, *Current Sci.*, 1938, **6**, 606.

¹³ *Ber.*, 1937, **70**, 788.

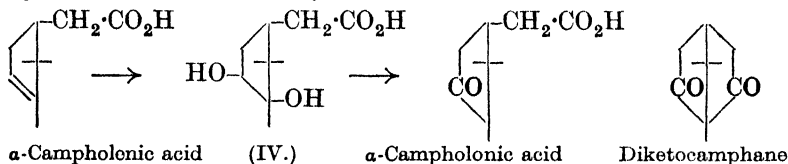
lead salt of this acid then gave *dl*-verbanone, which can be reduced to pinane, as already shown by H. Wienhaus and P. Schumm.¹⁴ *dl*- δ -Pinene was prepared by the reduction of verbanone to the alcohol, which was then dehydrated :



A new synthesis of *dl*-fenchone from camphenonic acid is described by G. Komppa and A. Klami.¹⁵ The acid is converted successively into the acyl chloride, aldehyde (hydrogen and palladium-barium sulphate), and alcohol (hydrogen, platinum dioxide, and ferrous sulphate) (III.); the last-named compound yields fenchone when its chloride is reduced :



Campholenic Acid, etc.—According to F. Tiemann,¹⁶ when α -campholenic acid is oxidised, one of the products is pinonic acid; such a reaction, however, would involve a change from the *cyclopentane* to the *cyclobutane* system and would be unique in terpene chemistry. G. Komppa and S. Beckmann¹⁷ could not confirm Tiemann's results: the first oxidation product of campholenic acid is the dihydroxy-acid (IV), which, when heated with dilute sulphuric acid, gives α -campholenic acid and 2 : 6-diketocamphane. Contrary to Tiemann's statement the acid does not give bromoform with sodium hypobromite, and the 2 : 6-diketocamphane is identical with that obtained by Y. Asahina, M. Ishidate, and T. Takamoto¹⁸ by the oxidation of *l*-bornyl acetate :



Sulphocamphylic Acid and the Camphylic Acids.—The structure of sulphocamphylic acid, obtained by the action of sulphuric acid on camphoric acid, and those of the α - and β -camphylic acids, produced from the sulpho-acid by fusion with alkaline hydroxides, have

¹⁴ *Annalen*, 1924, **439**, 20.

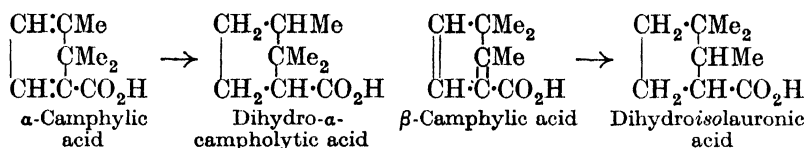
¹⁵ *Ber.*, 1935, **68**, 2001.

¹⁶ *Ibid.*, 1896, **29**, 3014.

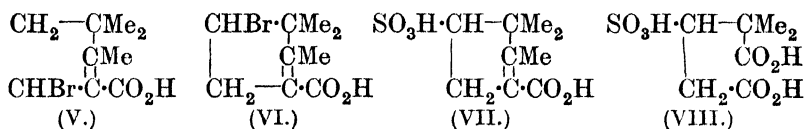
¹⁷ *Ibid.*, 1936, **69**, 2783.

¹⁸ *Ibid.*, p. 349.

been reinvestigated by J. R. Lewis and J. L. Simonsen.¹⁹ Both the camphylic acids absorb two molecules of hydrogen in the presence of a catalyst, the former yielding dihydro- α -campholytic acid and the latter dihydroisolauroic acid; both form additive products with α -naphthaquinone and both on ozonolysis give methyl *iso*-propyl ketone and oxalic acid. On the basis of these results the structures shown below are assigned to α - and β -camphylic acids :



With hydrogen bromide β -camphylic acid yields *isobromodihydro*- β -camphylic acid, to which the structure (V) is assigned on the basis of its decomposition into bromoform and *as*-dimethylsuccinic acid by ozonolysis, followed by treatment with sodium hypobromite :



When sulphocamphylyl bromide is heated, bromodihydro- β -camphylic acid is obtained; this product, as now shown, yields bromoform and *trans*- $\alpha\alpha$ -dimethylglutaconic acid on successive treatment with ozone and sodium hypobromite and therefore must be (VI), as the only other possible formula (V) has already been assigned. The structure (VII) for sulphocamphylic acid, suggested by the foregoing results, is thus established; moreover, the so-called sulphopimelic acid (VIII),²⁰ obtained by oxidation of (VII) with nitric acid, gives, when heated, *cis*- and *trans*-dimethylglutaconic acids and not terebic acid as supposed by Koenigs.

"Camphenilene" and Related Compounds.—P. Snitter²¹ described a hydrocarbon, "camphenilene," prepared from camphenilol and from camphenilyl chloride, as a crystalline solid, m. p. 26.5°; he concluded, solely on the evidence of the Raman spectrum, that it was a slightly impure sample of a compound of the structure (IX). Previously it had been shown that the "camphenilene" obtained in the same way by W. Jagelki and by S. V. Hintikka and G. Komppa²²



¹⁹ J., 1936, 734; 1937, 457.

²⁰ J. Kachler, *Annalen*, 1873, **169**, 179; W. Koenigs and J. Hoerlin, *Ber.*, 1893, **26**, 812, 2045.

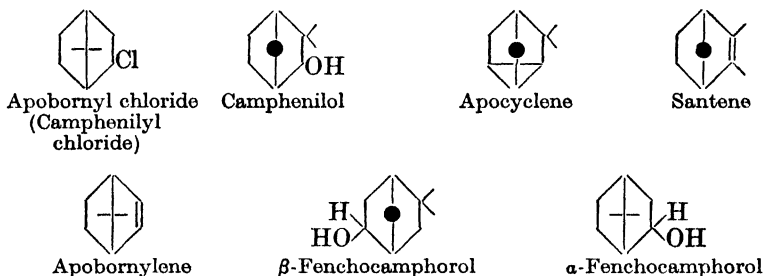
²¹ *Bull. Inst. Pin.*, 1933, 209.

²² *Ber.*, 1899, **32**, 1503; *Annalen*, 1912, **387**, 292.

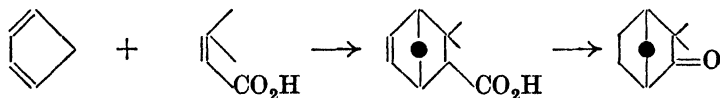
consisted mainly of santene.²³ Now, if the structure (IX) were correct, it would provide the first exception to the Bredt rule.²⁴ Snitter's camphenilene was therefore reinvestigated by G. Gratton and J. L. Simonsen,²⁵ who proved conclusively that it is mainly santene, together with a little apocyclene. The same conclusion was reached by G. Komppa and G. A. Nyman.²⁶

These facts show the unreliability of purely physical methods for the determination of structure and throw grave doubt, for example, on the work of G. Dupont and R. Dulon,²⁷ where such evidence is also used for the determination of the constitutions of the pyrolysis products of α -pinene.

P. Lipp and J. Daniels²⁸ have now shown that camphenyl chloride with sodium phenoxide gives mainly apobornylene; they could not detect any santene in their product. G. Komppa and G. A. Nyman²⁹ conclude from a study of the hydrolysis of "camphenyl chloride" with lime that the compound is mainly apobornyl chloride, since camphenilol, β -fenchocamphorol and α -isofenchocamphorol (a stereoisomeride of α -fenchocamphorol) are thereby produced. Similarly 4-methylcamphenilol gives mainly epibornyl chloride with phosphorus pentachloride.



An interesting synthesis of camphenilone is described by G. Komppa and O. Komppa:³⁰ cyclopentadiene is condensed with $\beta\beta$ -dimethylacrylic acid, and, after the catalytic reduction of the ethylenic linkage in the product, the acid is converted successively into the azide, amine and alcohol. The alcohol is then oxidised to a mixture which contains camphenilone:



²³ G. Komppa and S. V. Hintikka, *Bull. Soc. chim.*, 1917, [iv], **21**, 147.

²⁴ J. L. Simonsen, "The Terpenes," II, 154.

²⁵ *J.*, 1935, 1621.

²⁷ *Compt. rend.*, 1935, **201**, 219.

²⁸ *Ibid.*, p. 1813.

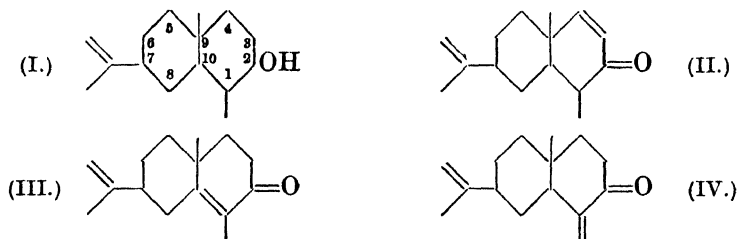
²⁶ *Ber.*, 1936, **69**, 334.

²⁹ *Ber.*, 1936, **69**, 586.

³⁰ *Ibid.*, p. 2606.

Sesquiterpenes.

Cyperones.—The main constituent of oil of *Cyperus rotundus* is a ketone, *d*- α -cyperone, $C_{15}H_{22}O$, which is readily purified with the aid of its semicarbazone.³¹ Catalytic hydrogenation converts cyperone into a tetrahydro-derivative, and reduction with sodium and alcohol yields dihydro- α -cyperol; this alcohol yields eudalene when it is heated with selenium, and a keto-alcohol, together with formaldehyde, on ozonolysis. Furthermore dihydro- α -cyperyl 3 : 5-dinitrobenzoate, on ozonolysis, gives a ketone which yields iodoform with Fuson's reagent.³² The isoprene rule being assumed valid, this evidence indicates the structure of the carbon skeleton, the conjugation of one double bond with the carbonyl group, and the presence of the second ethylenic linkage as $-C(CH_3):CH_2$. The alcohol formed from tetrahydro- α -cyperone and methylmagnesium iodide yields 1 : 2-dimethyl-7-isopropyl-naphthalene when it is dehydrogenated, a fact which indicates position 2 for the keto-group of cyperone; dihydro- α -cyperol must therefore be represented by (I) and cyperone by (II), (III) or (IV) :



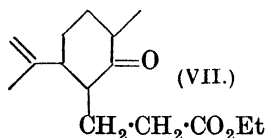
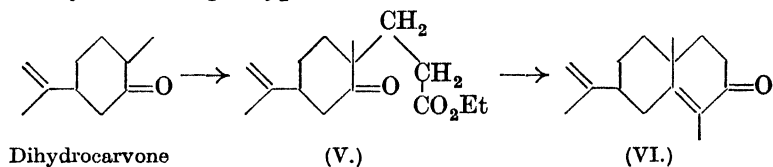
α -Cyperone yields a hydroxymethylene derivative which, by reduction and dehydrogenation, gives 1 : 3-dimethyl-7-isopropyl-naphthalene; the structure of this is proved by synthesis,³³ and its formation excludes formula (II) for cyperone. Structure (IV) is inadmissible, as the ozonolysis of α -cyperone semicarbazone gives a product, $C_{15}H_{23}O_4N_3$, whereas the semicarbazone of (IV) would clearly lose two carbon atoms when thus oxidised; α -cyperone is therefore represented by (III). β -Cyperone, which is formed by the action of aqueous oxalic acid on the α -ketone, is regarded as a stereoisomeride, since its semicarbazone and that of α -cyperone give the same degradation products. Substances structurally identical with cyperone have been synthesised by two independent

³¹ B. H. Hegde and B. S. Rao, *J. Soc. Chem. Ind.*, 1935, **54**, 387r; A. E. Bradfield, B. H. Hegde, B. S. Rao, J. L. Simonsen, and A. E. Gillam, *J.*, 1936, 667.

³² R. C. Fuson and C. W. Tullock, *J. Amer. Chem. Soc.*, 1934, **56**, 1638.

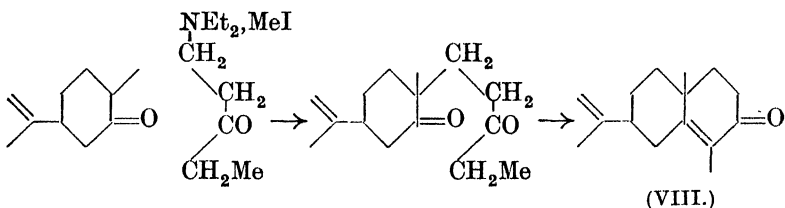
³³ A. E. Bradfield, R. R. Pritchard, and J. L. Simonsen, *J.*, 1937, 763.

methods,³⁴ which are of importance as furnishing the only direct evidence for the existence of the angle methyl group at position 9 in those sesquiterpenes which give eudalene on dehydrogenation. In one synthesis the condensation of the sodium derivative of *l*-dihydrocarvone with ethyl β -chloropropionate yielded (V); this product, with zinc and ethyl α -bromopropionate, gave a mixture of which the main fraction afforded on hydrolysis a ketone (VI), closely resembling β -cyperone :



The substance (V) was purified from any (VII) it might contain by means of its alkali-soluble condensation product with ethyl oxalate (cf. ref. 35).

The second cyperone synthesis is more direct and consists in the condensation of the methiodide of 1-diethylaminopentan-3-one with *l*-dihydrocarvone, in the presence of sodamide: the resulting diketone is readily cyclised to (VIII) :



The complete identity (structural and configurational) of the synthetic products (VI) and (VIII), made respectively at Bangor and at Oxford, with one another and with natural cyperone is not claimed, but sufficient similarity in the properties of various derivatives establishes the validity of the above structures.

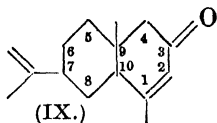
Eremophilone and Hydroxyeremophilone.—It was considered in 1932³⁶ that the structures of the three ketones, eremophilone, hydroxyeremophilone and hydroxydihydroeremophilone, had been decided. During the investigation of α -cyperone, however, it became necessary to prepare 1 : 3-dimethyl-7-isopropyl-naphthalene (p. 273)

³⁴ P. S. Adamson, F. J. McQuillin, R. Robinson, and J. L. Simonsen, *J.*, 1937, 1576.

³⁵ A. E. Bradfield, E. R. Jones, and J. L. Simonsen, *J.*, 1936, 1137.

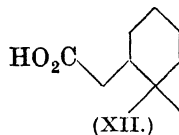
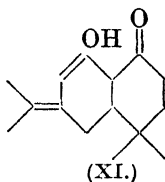
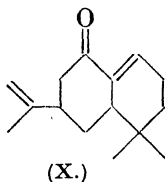
³⁶ *Ann. Reports*, 1932, 29, 155.

in order to identify it with the substance formed by the dehydrogenation of the reduction product of hydroxymethylene- α -cyperone. The simplest way to do this appeared to be by the dehydrogenation of the alcohol formed from eremophilone [then considered to be (IX)] with the aid of methylmagnesium iodide. It was then found



that the two naphthalene derivatives were not identical and, the structure of the product from cyperone having been decided by synthesis (above), it was proved by subsequent work that the compound from eremophilone is 1 : 5-

dimethyl-7-*isopropyl*naphthalene.³⁷ The position of the carbonyl group of eremophilone is thus fixed at 5 and not at 3. A confirmation of this evidence is afforded by the fact that hydroxymethylene-eremophilone yields 1 : 6-dimethyl-7-*isopropyl*naphthalene on reduction and dehydrogenation. It has also been shown³⁶ that the eremophilone structure contains a double bond conjugated with that of the carbonyl group. Now, if the carbonyl group is at position 5, and the methylene group at 6 (formation of hydroxymethylene derivative, etc.), it would be impossible to have an $\alpha\beta$ -ethylenic linkage (4 : 9) *together* with the angle methyl group at 9, a position assigned to it on account of the formation of eudalene from eremophilone. A reinvestigation of the ozonolysis of hydroxy-



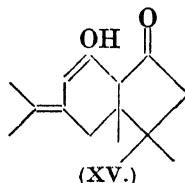
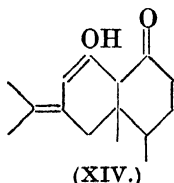
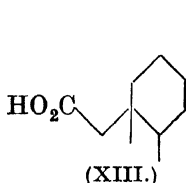
eremophilone benzoate³⁷ has shown that the final product of the prolonged action of ozone is a keto-acid, $C_{10}H_{16}O_3$, which is isolated as its semicarbazone, $C_{11}H_{19}O_3N_3$ (not $C_{13}H_{17}O_4N_3 \cdot 2C_2H_6O$ as previously assumed³⁸); this keto-acid is reduced to a saturated acid, $C_{10}H_{18}O_2$, by the Clemmensen method. Now, if the assumption of a head-to-tail isoprene arrangement is abandoned, formulæ (X) and (XI) are possible for eremophilone and hydroxyeremophilone respectively, and the acid $C_{10}H_{18}O_2$ would then be (XII).

2 : 2-Dimethylcyclohexylacetic acid was therefore synthesised, but it was different from the acid derived from hydroxyeremophilone; the suggested structures must therefore be dismissed unless it be assumed that a methyl group migrates at some stage. It was

³⁷ A. E. Bradfield, N. Hellström, A. R. Penfold, and J. L. Simonsen, *J.*, 1938, 767.

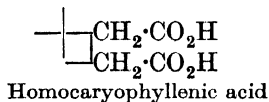
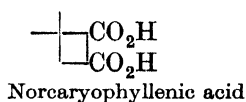
³⁸ A. E. Bradfield, A. R. Penfold, and J. L. Simonsen, *J.*, 1932, 2756.

subsequently shown³⁹ that the methyl ester of the acid $C_{10}H_{18}O_2$ yields *o*-xylene when it is dehydrogenated with selenium; the acid is therefore (XIII) and its formation from (XI) would be extremely unlikely. The most probable formula for hydroxyeremophilone thus appears to be (XIV), in which the isoprene rule is not followed;



other evidence that this is possible in the polyterpene series can be advanced.⁴⁰ It would also appear that formula (XV) (previously suggested by Simonsen³⁷), which is made up of isoprene residues, although not in the familiar head-to-tail arrangement, might account for the facts if it be assumed that during dehydrogenation the angle methyl is eliminated and a ring widening at the *gem*-dimethyl group occurs; in the present state of our knowledge such changes appear by no means impossible.⁴¹ Ring widening could also occur during the dehydrogenation of the ester of the acid $C_{10}H_{18}O_2$.

Caryophyllenes.—The syntheses and resolutions of the norcaryophyllenic acids by H. N. Rydon⁴² have now been followed by the conversion of *d*-*cis*-norcaryophyllenic acid into homocaryophyllenic acid by the ordinary ester reduction to the glycol, and the treatment of the latter with phosphorus tribromide, potassium cyanide and hydrolysing agents successively.⁴³



F. W. Semmler and E. W. Mayer,⁴⁴ by the oxidation of caryophyllene, isolated a keto-acid, $C_{11}H_{18}O_3$, from which, by the action of sodium hypobromite, L. Ruzicka and A. H. Wind⁴⁵ and C. R. Ramage and J. L. Simonsen⁴⁶ prepared a homocaryophyllenic acid. From a comparison of the dianilides of the natural and the synthetic acid it is now thought⁴³ that they are probably identical, but a

³⁹ J. L. Simonsen, private communication.

⁴⁰ J. C. E. Simpson, *J.*, 1938, 1313.

⁴¹ *Ann. Reports*, 1936, **33**, 294; N. N. Chatterjee, *J. Indian Chem. Soc.*, 1936, **13**, 588.

⁴² *J.*, 1936, 593; 1937, 1340; *Ann. Reports*, 1935, **32**, 325.

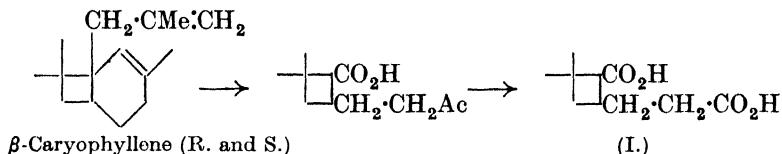
⁴³ C. R. Ramage and J. L. Simonsen, *J.*, 1937, 73.

⁴⁴ *Ber.*, 1911, **44**, 3662.

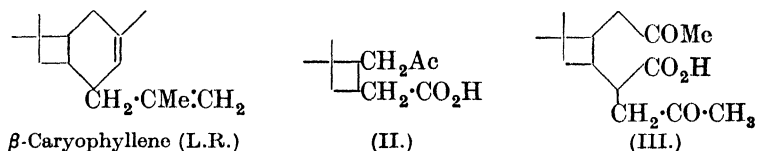
⁴⁵ *Helv. Chim. Acta*, 1931, **14**, 422.

⁴⁶ *J.*, 1936, 742.

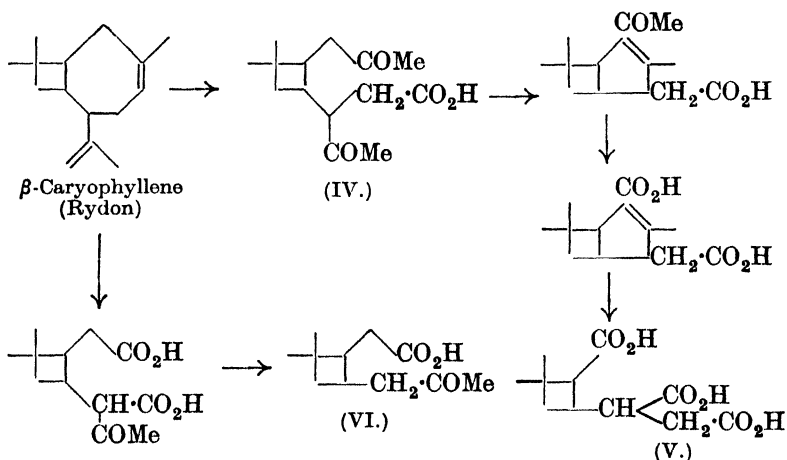
definite conclusion cannot be reached. The validity of the above structure for homocaryophyllenic acid being granted, Ramage and Simonsen's structure for β -caryophyllene⁴⁷ must now be abandoned, as it would give (I) for homocaryophyllenic acid :



Ruzicka's structure⁴⁸ accounts satisfactorily for the formation of homocaryophyllenic acid, of the keto-acid (II), and of a diketoid, $C_{14}H_{22}O_4$ (III), which forms the chief product of the ozonolysis of caryophyllene :



On the other hand, a ketone, $C_{10}H_{18}O$, and a diketone, $C_{13}H_{22}O_2$, which are also oxidation products, cannot be satisfactorily derived from this structure; the formation of clovene by isomeric change



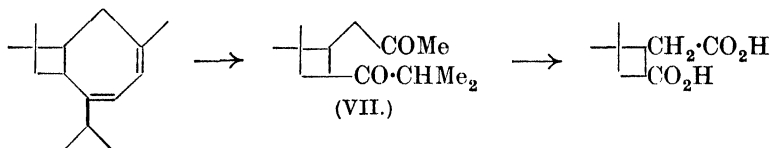
and its oxidation to an acid without the loss of carbon would also be hard to explain. There is, however, no evidence that these ketones are not derived from α -caryophyllene, which may be present even in the most highly purified samples of β -caryophyllene, and it

⁴⁷ *J.*, 1935, 1581; *Ann. Reports*, 1935, 32, 327.

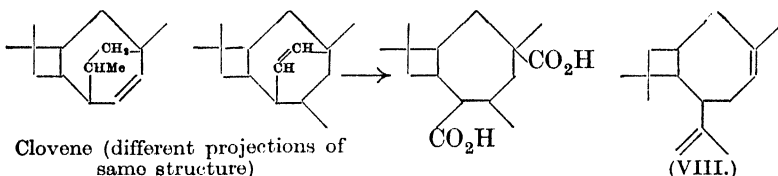
⁴⁸ *J. Soc. Chem. Ind.*, 1935, **54**, 509.

is therefore unsound to consider them in a discussion of the structure of β -caryophyllene. H. N. Rydon,⁴⁹ stimulated by recent work on the azulenes,⁵⁰ suggests for caryophyllene the structure shown below. The diketone-acid, $C_{14}H_{22}O_4$, would then become (IV) and it could be degraded finally to (V), in conformity with the results of L. Ruzicka, W. Zimmermann, and K. Huber.⁵¹

The formation of the keto-acid, $C_{11}H_{18}O_3$ (VI), is also explained. For the production of the diketone, $C_{13}H_{22}O_2$ (VII), Rydon assumes the presence of an isomeric caryophyllene :



The formation of the tricyclic clovene and its oxidation product, clovenic acid, would be easily accounted for :



On the other hand, clovenic acid readily yields an anhydride but it cannot be brominated. These facts are obviously not in accordance with Rydon's structure. An equally good formula for caryophyllene is (VIII) and a decision between these alternatives would be possible if the structure of caryophyllenic acid were determined. By the oxidation of acetamidodihydrocaryophyllene, a crystalline ketone has been prepared with the carbonyl group in the tail; it is hoped that the degradation of this compound will yield valuable results.⁵²

Betulenols.—Three closely related sesquiterpene alcohols, α -, β - and γ -betulenols, have been isolated from birch-bud oil by fractional reaction with phthalic anhydride.⁵³ All these alcohols yield a monocyclic dicarboxylic acid, betulenolic acid, $C_{10}H_{16}O_4$, on vigorous oxidation with permanganate, followed by nitric acid; this product gives a dimethyl ester which is easily hydrolysed by $N/10$ -alcoholic potassium hydroxide and therefore does not contain a tertiary carboxyl group; further oxidation gives oxalic and $\alpha\alpha$ -dimethylsuccinic acids.

⁴⁹ *J. Soc. Chem. Ind.*, 1938, **57**, 123.

⁵⁰ *Ann. Reports*, 1937, **34**, 396.

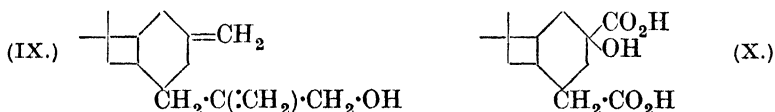
⁵¹ *Helv. Chim. Acta*, 1936, **19**, 343.

⁵² C. R. Ramage and J. L. Simonsen, private communication.

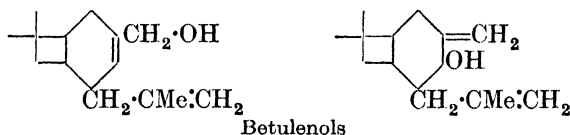
⁵³ *Ber.*, 1938, **71**, 612.

The identity of betulenolic acid with natural homocaryophyllenic acid has been proved by Simonsen and Ramage⁴³ and by W. Treibs.⁵³

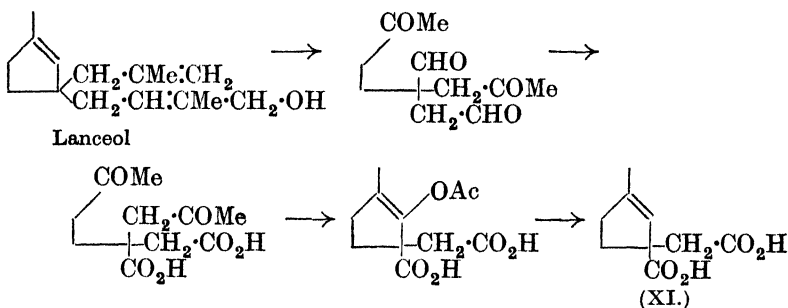
The chief component of birch-bud oil, the α -alcohol, can be oxidised to a saturated dicyclic hydroxy-dicarboxylic acid, $C_{13}H_{20}O_5$, which on further oxidation gives betulenolic acid; on this basis α -betulenol has the formula (IX) and the acid, (X), the structure discussed above for homocaryophyllenic acid being assumed :



The following formulæ are suggested for the isomeric betulenols :



Lanceol.—This sesquiterpene alcohol, $C_{15}H_{24}O$, was first isolated from the wood of *Santalum lanceolatum* by A. R. Penfold :⁵⁴ the usual methods now show that it is a primary monocyclic alcohol containing three ethylenic linkages, which are not conjugated.⁵⁵ When it is oxidised with ozone, formaldehyde and hydroxyacetone are found in the portion volatile in steam; the latter was identified as its



osazone, and the possibility of methylglyoxal being present is eliminated by the fact that the double bonds are not conjugated. The non-volatile portion, on further oxidation with silver oxide, yields lævulinic acid, and a crystalline acid, $C_9H_{12}O_4$, which on ozonolysis is converted into δ -acetylbutane- $\alpha\beta$ -dicarboxylic acid. From a consideration of all the structures which could yield this

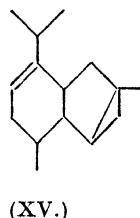
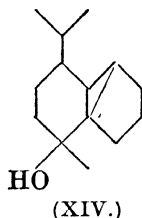
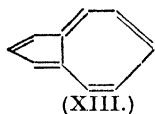
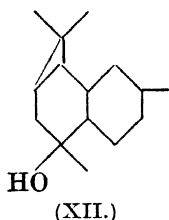
⁵⁴ J. Proc. Roy. Soc., N.S.W., 1928, **62**, 60; 1932, **66**, 240.

⁵⁵ A. E. Bradfield, E. M. Francis, A. R. Penfold, and J. L. Simonsen, J., 1936, 1619.

acid on ozonolysis it is finally concluded that the acid $C_9H_{12}O_4$ is probably (XI): some of the alternatives were excluded by a comparison of the acid $C_9H_{12}O_4$ with synthetic acids.

The structure shown is then advanced for lanceol and the formation of (XI) from it is explained as above. An alternative structure containing an *isopropylidene* instead of an *isopropenyl* group would yield (XI) directly on ozonolysis, the *cyclopentene* ring being assumed to be unattacked; the failure to detect acetone among the products of oxidation, however, renders such an alternative unlikely.

Ledol.—The constitution previously advanced for ledol (XII)⁵⁶ has been amended by G. Komppa and G. A. Nyman⁵⁷ on the ground of the dehydrogenation of ledol to azulenes [skeleton (XIII)]. It is pointed out that a substance (XII) would be expected to yield cadalene on dehydrogenation; this is actually only a minor product. If, however, the *cyclopropane* ring is present as in (XIV), the formation of an azulene is readily explained on the assumption that during dehydrogenation the bond between the carbon atoms common to the two rings undergoes fission, giving a 7:5 dicyclic structure.



This view is supported by the fact that copaene (XV) does not give azulene on dehydrogenation.

Irone.—The classical work of F. Tiemann and P. Krüger⁵⁸ on irone and its dehydration product, irene, led to erroneous conclusions with regard to the structures of these compounds, as was first shown by L. Ruzicka, C. F. Seidel, and H. Schinz;⁵⁹ these investigators proved that irone is $C_{14}H_{22}O$ (and not $C_{13}H_{20}O$) and that irene is $C_{14}H_{20}$. Irene yields 1:2:6-trimethylnaphthalene on dehydrogenation and from this fact, and other evidence, is assigned the constitution (XVII). This structure has now been confirmed by a synthesis of irene by M. T. Bogert and P. M. Appelbaum.⁶⁰ *m*-Tolylmagnesium bromide, with ethylene oxide, gave β -*m*-tolyl-

⁵⁶ G. Komppa, *Norske Vidensk. Selsk. Skr.*, 1933, 1.

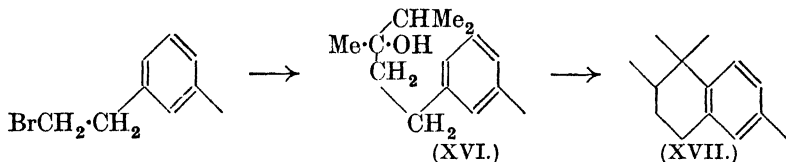
⁵⁷ *Compt. rend. Trav. Lab. Carlsberg*, 1938, 22, 272.

⁵⁸ *Ber.*, 1893, 26, 2675; 1895, 28, 1754.

⁵⁹ *Helv. Chim. Acta*, 1933, 16, 1143.

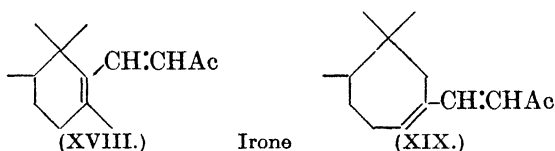
⁶⁰ *J. Amer. Chem. Soc.*, 1938, 60, 930.

ethanol, and the Grignard reagent of the corresponding bromide yielded, with methyl *isopropyl* ketone, the tertiary alcohol (XVI). When this alcohol was heated with sulphuric acid, 1:1:2:6-tetramethyltetralene (XVII) was formed, which was proved to be



identical with irene, obtained from irone, both by a comparison of their physical properties and by a study of their oxidation products.

Ruzicka and his co-workers (*loc. cit.*) advanced two possible structures for irone, (XVIII) and (XIX): the former explains the formation of irene in a simple manner but is difficult to reconcile with the production of $\beta\beta\gamma$ -trimethylpimelic acid by the ozonolysis of irone; the latter (XIX) would account readily for the production of this acid but not for the formation of irene.



F. B. K.

6. STEROIDS.

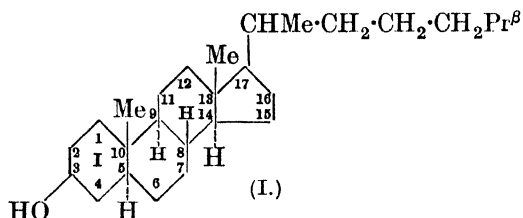
Stereoisomerism and Nomenclature.—Before considering the preparative work which has been carried out in the field of steroid chemistry during the last two years, it is appropriate to consider a major theoretical problem which is slowly being cleared up concurrently with these detailed investigations, namely, that of the spatial configuration of substituent groups in steroids, and to give some attention to the vexing question of nomenclature of stereoisomeric compounds, which, as a result of the attempts to reduce confusion by introducing new systems, is acquiring a chaotic appearance to observers outside the field.

Much of the latest stereochemical theory of the steroids is due to L. Ruzicka and his co-workers, who, in a series of papers ¹ have dealt with the assignment of configuration, relative to adjacent

¹ L. Ruzicka, *Helv. Chim. Acta*, 1933, **16**, 327; 1934, **17**, 1407; L. Ruzicka, M. W. Goldberg, J. Meyer, H. Brüngger, and E. Eichenberger, *ibid.*, 1934, **17**, 1395; L. Ruzicka, M. W. Goldberg, and H. Wirz, *ibid.*, 1935, **18**, 61; L. Ruzicka and M. W. Goldberg, *ibid.*, 1936, **19**, 99; L. Ruzicka and H. Kägi, *ibid.*, 1936, **19**, 842; 1937, **20**, 1557; cf. *Ann. Reports*, 1934, **31**, 207.

centres of asymmetry, to epimeric steroid alcohols with hydroxyl groups in positions 3 or 17, and to the junctions of the rings.

In view of the complexity of the matter, no apology is needed for recapitulating the theory now generally accepted. Practically all known steroid compounds belong to one of two ring-systems: (1) the cholestane, *allocholane*, *allopregnane*, or androstane type, or (2) the coprostanane, *cholane*, *pregnane*, or *aetiocholane* type. These differ in the orientation of the hydrogen on C_5 relative to the 10-methyl group, which is *trans* in type 1 and *cis* in type 2. Ruzicka's hypothesis assumes that cholestanol has the configuration (I), denoted by *trans*, *trans*—*anti*—*trans*—*anti*—*trans*.



Further, isomerism of 3-hydroxyl compounds *cis* or *trans* to the hydrogen on C_5 gives four sub-types: Ia (3-*trans*-OH, as in cholestanol); Ib (3-*cis*-OH, as in *epicholestanol*); IIa (3-*trans*-OH, as in *epicoprostanol*); IIb (3-*cis*-OH, as in *coprostanol*). The next type of isomerism found is that of 17-hydroxyl compounds, which may be *cis* or *trans* relative to the 13-methyl group. The configurations suggested have been supported by a series of chemical and physical observations in the papers mentioned, the most important generalisation being the Auwers-Skita rule applied to reduction of 3-ketones.

K. Miescher and W. H. Fischer² have expounded the application of the Auwers-Skita rule to the stereochemistry of epimeric alcohols with special reference to the steroids, and revealed how speculative the generalisations applying to epimeric *cycloparaffin* alcohols with one adjacent substituent in the ring may become when they are transferred to epimeric 3-hydroxysteroids in which there are three substituents. As a result, however, of reviewing the behaviour of the 3-hydroxysteroids, particularly in the light of their ability to form glucosides, it is concluded that compounds can be classified as "cisoid" (non-reactive hydroxyl group) or "transoid" (reactive hydroxyl group) in behaviour. The above authors suggest using these terms, abbreviated to "*c*" and "*t*," as prefixes to the names; thus cholestanol is *t*-cholestanol. The result is discordant with the Ruzicka "*cis*" and "*trans*" nomenclature only in the

² *Helv. Chim. Acta*, 1938, **21**, 336.

cases of coprostanol, which is *cis* but "transoid", and *epi*-coprostanol, which is *trans* but "cisoid." This anomaly is compared with that of the *cis*-decalols.

In the latest paper from Ruzicka's laboratory,³ the work of G. Vavon and B. Jakubowicz⁴ has been extended to examination of the rates of hydrolysis of the acetates and benzoates of four types of epimeric pairs: (a) cholestanol and *epi*cholestanol, (b) coprostanol and *epi*coprostanol, (c₁) 17-*trans*- and 17-*cis*-hydroxy-androstan-3-one, (c₂) 17-*trans*- and 17-*cis*-testosterone, and (d) cholesterol and *epi*cholesterol. All the compounds denoted as *trans* by Ruzicka were more readily hydrolysed than the *cis*-epimerides. Finally, when the assumed configurations are built up in a series of models, a mechanical explanation is apparent for the steric hindrance assumed to be responsible for the lowered reactivity in the cases in which it is found. The property of forming digitonides also can be correlated with the conformation of the molecule. The anomalous esterifications of Miescher and Fischer are dismissed for the reason that reactions not taking place in homogeneous solution may not be controlled by simple factors only.

The ancillary problem of nomenclature of stereoisomerides is in a controversial state. Definition of the configuration of the hydroxyl group at C₃ relative to a hydrogen atom at C₅, which is of variable configuration and in many cases is non-existent, as in Ruzicka's system, introduces difficulty and confusion. The alternative of using the methyl group at C₁₀ as a standard of reference, suggested by R. Schoenheimer and E. A. Evans⁵ and adopted in the last Report,⁶ has not won favour, particularly as some of the designations *cis* and *trans* become reversed. L. F. Fieser⁷ has suggested that "the configuration at C₃ common to cholesterol, dihydrocholesterol, coprosterol, ergosterol and similar steroids is appropriately designated where necessary by the classical prefix β , while the epimers of these substances are 3(α)-hydroxy-compounds, as are the bile acids and androsterone." Provided that the mistake responsible for the historical name " β -cholestanol" is ignored, and, further, that α and β are kept within parentheses, adjacent to a position numeral, and confusion with other uses of the Greek alphabet thus avoided, this proposal actually provides a convention for defining arbitrarily

³ L. Ruzicka, M. Furter, and M. W. Goldberg, *Helv. Chim. Acta*, 1938, **21**, 498.

⁴ *Bull. Soc. chim.*, 1933, [iv], **53**, 581.

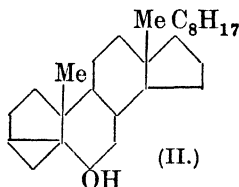
⁵ *J. Biol. Chem.*, 1936, **114**, 567; cf. R. K. Callow and F. G. Young, *Proc. Roy. Soc.*, 1936, **A**, **157**, 194.

⁶ *Ann. Reports*, 1936, **33**, footnote, p. 343.

⁷ "A Supplement to the Chemistry of Natural Products Related to Phenanthrene," New York, 1937, p. 399.

the position of the 3-hydroxyl group relative to the steroid skeleton as a whole. A. Butenandt⁸ uses the new prefix *n*- and the old term *epi*- in the same sense as (β)- and (α)-, respectively. Fieser's proposal, however, has been adopted by several workers, and an analogous system of labelling hydroxyl groups similarly oriented in a series of compounds has been extended to the 17.⁹ and the 20-positions¹⁰ in the pregnane skeleton. In this Report Fieser's system has been adopted for systematic names, whilst certain "trivial" names have been retained on account of their familiarity.

i-Cholesterol and the "Abnormal" Cholesteryl Ethers.—Isomerism which is to be explained on structural rather than spatial grounds occurs in the *i*-sterols, in which a novel and surprising form of molecular rearrangement has been postulated to explain the results of an attempt to epimerise the hydroxyl group of cholesterol. The work was based on that of W. Stoll¹¹ and of T. Wagner-Jauregg and L. Werner,¹² who described two series of isomeric ethers—(a) "normal," lævo-rotatory, and (b) "abnormal," strongly dextro-rotatory—formed when the *p*-toluenesulphonate, or the chloride or bromide of cholesterol reacted with alcohols (a) alone, or (b) in the presence of potassium acetate, respectively. The dextrorotation of the "abnormal" ethers was anomalous,¹³ and certain of their



properties were peculiar, if they were to be considered as derivatives of *epi*cholesterol. E. S. Wallis, E. Fernholz, and F. T. Gophart¹⁴ treated cholesteryl *p*-toluenesulphonate with potassium acetate in acetic anhydride and obtained the acetate of *i*-cholesterol, which was not identical with any of the known isomerides (*allo*-, *epi*-, or *epiallo*-) whose existence was explicable¹⁵ on the basis of epimerisation of the 3-hydroxyl group or shift of the ethylenic linkage from 5 : 6 to 4 : 5. *i*-Cholesterol exhibited no unsaturation. It was assigned the structure (II) with a bridge linking between C₃ and C₅.

J. H. Beynon, I. M. Heilbron, and F. S. Spring¹⁶ confirmed this work, and the analogy with the "abnormal" ethers, but did not accept the 6-position of the hydroxyl group. E. G. Ford, P.

⁸ Cf. A. Butenandt and G. Müller, *Ber.*, 1938, **71**, 191.

⁹ T. Reichstein and K. Gätzli, *Helv. Chim. Acta*, 1938, **21**, 1185.

¹⁰ R. E. Marker, O. Kamm, E. L. Wittle, T. S. Oakwood, E. J. Lawson, and J. F. Laucius, *J. Amer. Chem. Soc.*, 1937, **59**, 2291.

¹¹ *Z. physiol. Chem.*, 1932, **207**, 147; 1937, **246**, 13.

¹² *Ibid.*, 1932, **213**, 119.

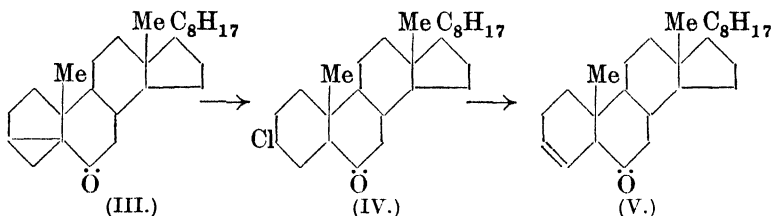
¹³ Cf. R. K. Callow and F. G. Young, *Proc. Roy. Soc.*, 1936, **A**, **157**, 194.

¹⁴ *J. Amer. Chem. Soc.*, 1937, **59**, 137.

¹⁵ Cf. *Ann. Reports*, 1936, **33**, 341.

¹⁶ *J.*, 1937, 1459.

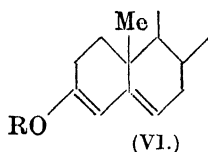
Chakravorty, and E. S. Wallis¹⁷ then reported the isolation of *i*-cholestanone (III), by oxidation of *i*-cholesterol. *i*-Cholestanone was converted successively into α -3-chloro-6-keto-cholestane (IV), "heterocholestenone" (V), and 6-ketocholestane, thus clinching the position of the oxygen atom. I. M. Heilbron, J. Hodges, and F. S. Spring¹⁸ accept this conclusion, but contest the intermediate stages, since they obtain "heterocholestenone," to which they assign the "*i*"-structure (III), directly from *i*-cholesterol, and



consider the *i*-cholestanone of the American workers inhomogeneous. Androstane and pregnane derivatives belonging to the *i*-series have been obtained by analogous methods.¹⁹

Enol Esters of Δ^4 -3-Keto-steroids.—Owing to the effect which esterification of sex hormone alcohols has in prolonging their physiological action when they are injected, numerous esters with acids of all types have been prepared.²⁰

Following this line of investigation, the preparation of the acetate



of the enolic form of cholestenone²¹ led to the preparation of enol esters of the hormones progesterone and testosterone,²² which were shown to have the Δ^3 :⁵-structure (VI) rather than the Δ^2 :⁴-structure. The expected pro-

traction of the biological activity was found with the testosterone compounds,²³ but not with those from progesterone.

E. Schwenk, G. Fleischer, and B. Whitman²⁴ report the prepara-

¹⁷ *J. Amer. Chem. Soc.*, 1938, **60**, 413.

¹⁸ *J.*, 1938, 759.

¹⁹ A. Butenandt and W. Grosse, *Ber.*, 1936, **69**, 2776; 1937, **70**, 1446.

²⁰ Cf. K. Miescher, A. Wettstein, and E. Tschopp, *Biochem. J.*, 1936, **30**, 1977; *Schweiz. med. Woch.*, 1936, **66**, 763; K. Miescher, H. Kägi, C. Scholz, A. Wettstein, and E. Tschopp, *Biochem. Z.*, 1937, **294**, 39; K. Miescher and C. Scholz, *Helv. Chim. Acta*, 1937, **20**, 263, 1237.

²¹ L. Ruzicka and W. H. Fischer, *Helv. Chim. Acta*, 1936, **19**, 806; H. H. Inhoffen, *Ber.*, 1936, **69**, 2141.

²² L. Ruzicka and W. H. Fischer, *Helv. Chim. Acta*, 1936, **19**, 1371; U. Westphal, *Naturwiss.*, 1936, **24**, 696; *Ber.*, 1937, **70**, 2128.

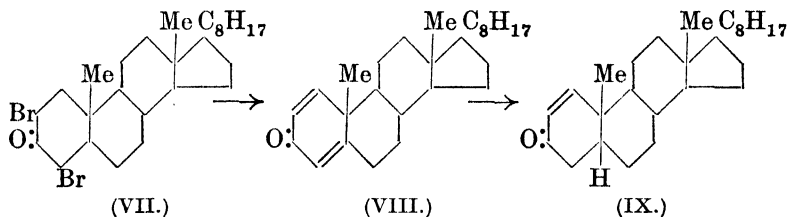
²³ K. Miescher, W. H. Fischer, and E. Tschopp, *Nature*, 1937, **140**, 726.

²⁴ *J. Amer. Chem. Soc.*, 1938, **60**, 1702.

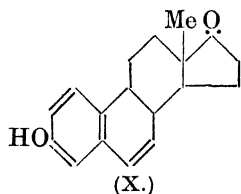
tion of the enol ethyl ethers from cholestenone and testosterone propionate and benzoate by interaction with ethyl orthoformate. I. M. Heilbron, T. Kennedy, F. S. Spring, and G. Swain²⁵ have prepared enol-acetates of ergostatrienone and lumistatrienone, spectroscopically identical, to which the $\Delta^{3:5:7}$ -structures are assigned, of ergostatetraenone ($\Delta^{3:5:7:9}$), and of *iso*ergostatrienone. The last-named compound is assigned the $\Delta^{2:4:6}$ -structure.

Bromination and Debromination.—Investigations on the bromination of sterol derivatives, having as their object the aromatisation of ring I, or, at least, the preparation of heavily unsaturated compounds, were referred to in the last Report, and these have continued actively.²⁶

H. H. Inhoffen and Huang-Minlon²⁷ have obtained the most promising result in preparing $\Delta^{1:4}$ -cholestadien-3-one (VIII) by debrominating 2:4-dibromocholestan-3-one (VII) with pyridine.



Partial hydrogenation yielded Δ^1 -coprostenone (IX). The authors consider both these compounds suitable starting materials for preparing steroids in which ring I is aromatic.



A preliminary announcement²⁸ has been made of the conversion of dibromoandrostanedione into products which on thermal decomposition give a phenol with weak oestrogenic activity which may be *iso*-equilin (X).

Preparation of Δ^4 -3-Ketones.—A general reaction which enables one to prepare the important Δ^4 -3-ketones from Δ^5 -3-hydroxy-compounds deserves particular mention, as its application to the preparation of testo-

²⁵ *J.*, 1938, 869.

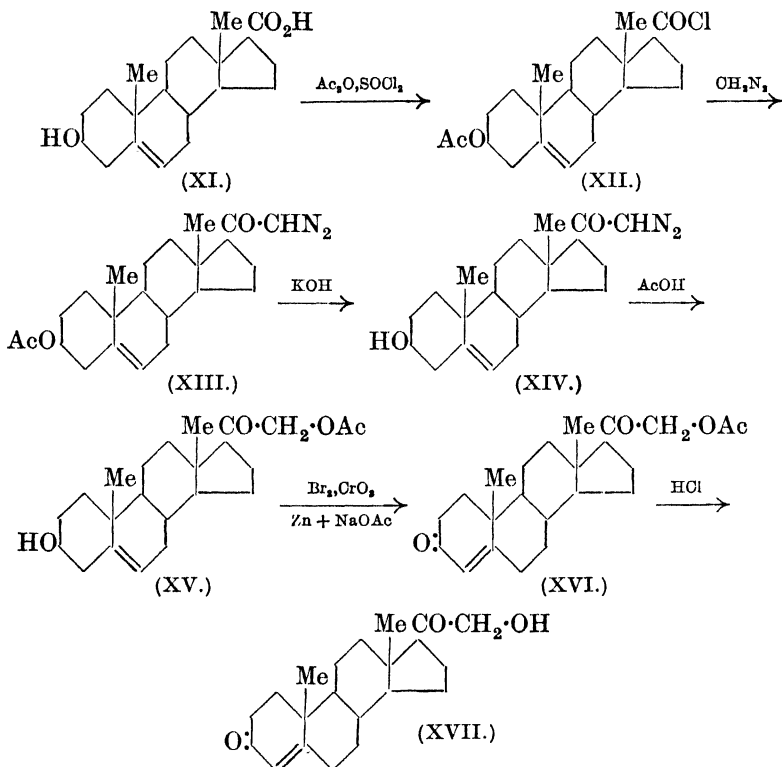
²⁶ *Ann. Reports*, 1936, **33**, 343; A. Butenandt, G. Schramm, and H. Kudssus, *Annalen*, 1937, **531**, 176; I. M. Heilbron, E. R. H. Jones, and F. S. Spring, *J.*, 1937, 801; I. M. Heilbron, H. Jackson, E. R. H. Jones, and F. S. Spring, *J.*, 1938, 102; T. Barr, I. M. Heilbron, E. R. H. Jones, and F. S. Spring, *ibid.*, p. 334; H. H. Inhoffen, *Ber.*, 1937, **70**, 1695; L. Ruzicka, P. A. Plattner, and R. Aeschbacher, *Helv. Chim. Acta*, 1938, **21**, 866; E. Schwenk and B. Whitman, *J. Amer. Chem. Soc.*, 1937, **59**, 949.

²⁷ *Ber.*, 1938, **71**, 1720.

²⁸ H. H. Inhoffen, *Naturwiss.*, 1937, **25**, 125.

sterone and progesterone or allied compounds has been of special value. The method of reducing ketones with aluminium alkoxides²⁹ is reversed with respect to the sterol, by suitable adjustment of the proportion of reactants, and the Δ^5 -hydroxy-compound is refluxed with a considerable excess of acetone, benzene, and aluminium *tert.*-butoxide.³⁰

New Degradations of the 17-Side-chain.—One more important



degradation has been added to the series of "partial syntheses" of hormones from sterols and bile acids. M. Steiger and T. Reichstein elaborated a method of preparing 3(β)-hydroxy- Δ^5 -aetiocholenic acid (XI) from stigmasterol³¹ and proceeded³² to build up the corticosterone side-chain in position 17 by the series of reactions shown (XI—XVII). The product, deoxycorticosterone, or 21-

²⁹ H. Meerwein and R. Schmidt, *Annalen*, 1925, **444**, 221; W. Ponndorf, *Z. angew. Chem.*, 1926, **39**, 138.

³⁰ R. V. Oppenauer, *Rec. Trav. chim.*, 1937, **56**, 137.

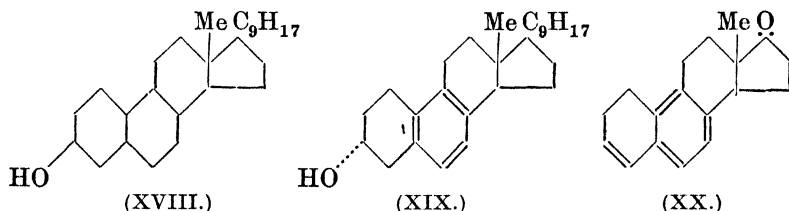
³¹ *Helv. Chim. Acta*, 1937, **20**, 1040.

³² *Nature*, 1937, **139**, 925; *Helv. Chim. Acta*, 1937, **20**, 1164.

hydroxyprogesterone, has recently³³ been found in adrenal extracts, though present in smaller amount than corticosterone. It is even more active than corticosterone and, in view of the high degree of specificity of this type of hormone activity to structure, this fact is accounted as evidence in favour of the assumed positions of three of the four oxygen atoms in corticosterone itself.

Degradations from sterols direct to the pregnane series have been reported by N. I. Tavastsherna³⁴ and by W. Dirscherl and F. Hanisch.³⁵ The latter authors oxidised cholestenone directly to progesterone with chromium trioxide, but the yield is not stated, and it might be inferred, from the activity in attempting to reach progesterone from other directions, that it is not good. The degradation of a saturated heart poison genin, *viz.*, periplogenin, to progesterone has been claimed in a patent.³⁶

The reported degradation of ergosterol to œstrone³⁷ has been controverted from more than one quarter. A. Windaus and M. Deppe³⁸ were unable to obtain from tetradehydroneoergosterol (XVIII) by the method of the American workers, a substance with ring I aromatic, and only isolated a product which they proved to be *epineoergosterol* (XIX).



P. N. Chakravorty and E. S. Wallis³⁹ confirmed the German work and oxidised *epineoergosterol* to a ketone, $C_{18}H_{20}O$, which may be 17-keto- $\Delta^{3:5:7:9}$ -œstratetraene (XX). R. E. Marker⁴⁰ has, however, defended his original work, firstly on the grounds of the analogous reduction of β -naphthol to *ar*-tetrahydro- β -naphthol in 8% yield by E. Bamberger and M. Kitschelt,⁴¹ and, secondly, by reporting the reduction of ring II of equilenin and of α - and β -dihydroequilenin. The crude reduction product of equilenin yielded œstrone on oxidation; α - and β -dihydroequilenin yielded α - and β -œstradiol,

³³ T. Reichstein and J. v. Euw, *Helv. Chim. Acta*, 1938, **21**, 1197.

³⁴ *Arch. biol. Nauk*, 1935, **50**, 141.

³⁵ *Z. physiol. Chem.*, 1938, **252**, 49.

³⁶ B.P. 482,321, 10.3.37. Switz., 23.3.36 and 9.2.37.

³⁷ R. E. Marker, O. Kamm, T. S. Oakwood, and J. F. Laucius, *J. Amer. Chem. Soc.*, 1936, **58**, 1503; *Ann. Reports*, 1936, **33**, 361.

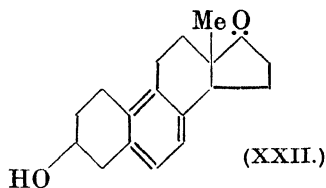
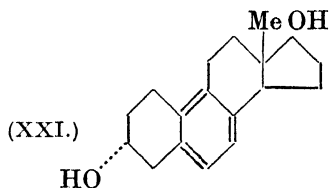
³⁸ *Ber.*, 1937, **70**, 76.

³⁹ *J. Amer. Chem. Soc.*, 1938, **60**, 1379.

⁴⁰ *Ibid.*, p. 1897.

⁴¹ *Ber.*, 1890, **23**, 885.

respectively. Experimental details of the reduction of tetrahydro-neoergosterol are promised for a later publication. L. Ruzicka, P. Müller, and E. Mörgeli⁴² report independent investigations on the same lines as those of Marker and his co-workers. They did, in fact, obtain up to 20% of phenolic material from the reduction of equilenin by sodium and amyl alcohol, but considered that the possibility of a practicable degradation of ergosterol to œstrone was too remote for the investigation to be continued. The hexahydro-equilenin they actually isolated, which they formulated as (XXI),



had no androgenic activity. The œstrogenic activity was so small that it was not consistent with the report by I. A. Remesov⁴³ that the substance obtained by degradation of neoergosterol, and formulated as 17-keto- $\Delta^{5:7:9}$ -œstratriene (XXII), possesses activity comparable with that of œstrone.

Transition from the Androstane to the Pregnane Series.—Since the interaction of methyl- and ethyl-magnesium halides with 17-keto-androstanes took place readily, it was natural that efforts should be made to introduce more reactive groups in the same way. S. Kuwada and M. Yago⁴⁴ described the reaction of vinylmagnesium bromide with Δ^5 -androst-3(β)-ol-17-one ("trans-dehydroandrost-erone") and claimed the formation of 17-vinyl- Δ^5 -androstene-3(β):17-diol, but this work cannot be confirmed.⁴⁵ A. Butenandt and D. Peters,⁴⁵ however, have started a very promising series of reactions with interaction of the acetate with allylmagnesium bromide. The 17-allylandrostenediol so obtained was converted by an Oppenauer oxidation³⁰ into 17-allylt testosterone, from which was obtained the 17:21-diene, the 17:20:21:22-tetrol, and two isomeric 17:21:22-triols which differed in the configuration at C₂₁, since they gave the same 20-aldehyde. W. A. Yarnall and E. S. Wallis⁴⁶ claimed to have condensed ethyl α -chloropropionate with Δ^5 -androst-3(β)-ol-17-one and to have converted the product into pregnane derivatives, but the work has not yet been confirmed,

⁴² *Helv. Chim. Acta*, **21**, 1394.

⁴³ *Bull. Exp. Biol. Med.*, 1936, **1**, 181; *Rec. Trav. chim.*, 1936, **55**, 797.

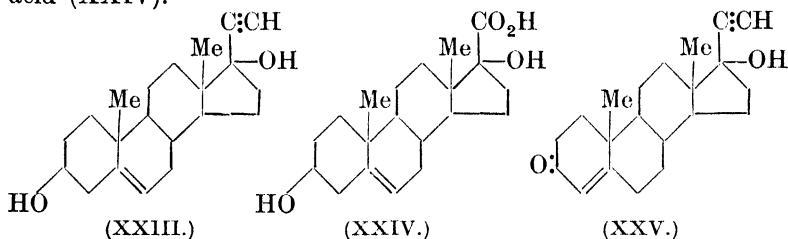
⁴⁴ *J. Pharm. Soc. Japan*, 1936, **56**, 109; *Chem Zentr.*, 1937, **1**, 3808.

⁴⁵ L. Ruzicka, K. Hofmann, and H. F. Meldahl, *Helv. Chim. Acta*, 1938, **21**, 371; A. Butenandt and D. Peters, *Ber.*, 1938, **71**, 2688.

⁴⁶ *J. Amer. Chem. Soc.*, 1937, **59**, 951.

nor have experimental details been published. Another form of Darzens condensation, with ethyl dichloroacetate, was attempted by A. Ercoli and L. Mamoli,⁴⁷ but only the ester was obtained.

The addition of acetylene to the 17-carbonyl group was achieved independently by J. Kathol, W. Logemann, and A. Serini⁴⁸ and by L. Ruzicka and K. Hofmann.⁴⁹ The latter authors condensed potassium acetylide in liquid ammonia with Δ^5 -androstene-3(β)-ol-17-one ("trans-dehydroandrosterone") and androstan-3(β)-ol-17-one to give the corresponding 17-ethynyl-17-hydroxy-compounds. Subsequently⁵⁰ 17-ethynyl- Δ^5 -androstene-3(β):17-diol (XXIII) was converted by ozonisation, after protection of the hydroxyl group and the ethylenic linkage, into 3(β):17-dihydroxy- Δ^5 -actiocholenic acid (XXIV).



L. Ruzicka, K. Hofmann, and H. F. Meldahl⁵¹ converted (XXIII) by reduction into the vinyl derivative, and by oxidation with aluminium *tert.*-butoxide into ethinyldiandrosterone (XXV), a substance with the physiological properties of progesterone. Vinyltestosterone was prepared by L. Ruzicka, K. Hofmann, and H. F. Meldahl⁵² by analogous methods.

Another route to pregnane derivatives from ethinylandrostane compounds is reported by L. Ruzicka and H. F. Meldahl,⁵³ who found that 17-ethynyl- Δ^5 -androstene-3(β):17-diol in glacial acetic acid in the presence of acetic anhydride and mercuric oxide together with the boron fluoride-ether catalyst⁵⁴ readily added on acetic acid and gave rise to 3(β):17-diacetoxy- Δ^5 -pregnen-20-one (XXVI). The goal of the investigation, the preparation of 17-hydroxyprogesterone, was attained (a) by partial saponification of (XXVI) to the 17-monoacetate and oxidation by Oppenauer's method, or (b) by addition of acetic acid to 17-ethinyldiandrosterone (XXV).

H. H. Inhoffen, W. Logemann, W. Hohlweg, and A. Serini⁵⁵

⁴⁷ *Chim. e l'Ind.*, 1937, **19**, 435.

⁴⁸ *Naturwiss.*, 1937, **25**, 682.

⁴⁹ *Helv. Chim. Acta*, 1937, **20**, 1280.

⁵⁰ *Ibid.*, 1938, **21**, 88.

⁵¹ *Ibid.*, p. 371.

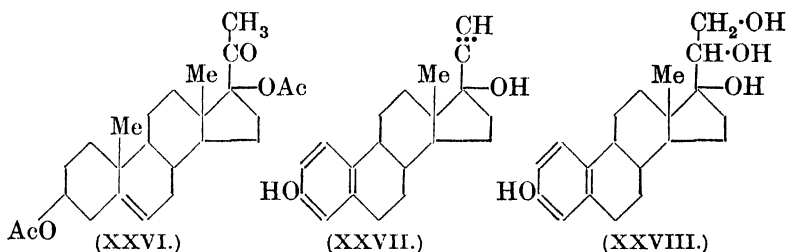
⁵² *Ibid.*, p. 597.

⁵³ *Ibid.*, p. 1760.

⁵⁴ G. F. Hennion, H. D. Hinton, and J. A. Nieuwland, *J. Amer. Chem. Soc.*, 1933, **55**, 2858.

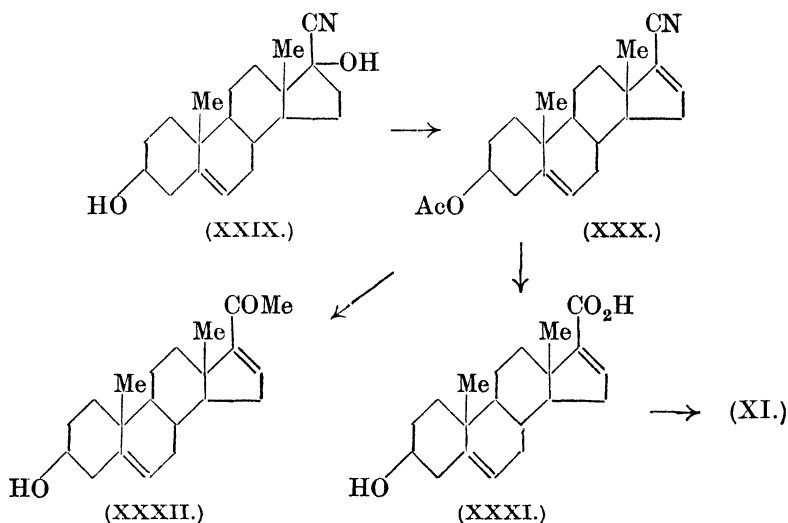
⁵⁵ *Ber.*, 1938, **71**, 1024; cf. H. H. Inhoffen and W. Hohlweg, *Naturwiss.*, 1938, **26**, 96.

applied the process of acetylene condensation to œstrone, equilin, and equilenin and obtained the corresponding ethynyl compounds.



17-Ethynylœstratriene-3 : 17-diol (XXVII) was converted by reduction into the vinyl compound, and the latter by osmium tetroxide oxidation into 17-(α -dihydroxyethyl)œstradiol (XXVIII).

S. Kuwada and M. Miyasaka⁵⁶ attacked the problem of attaching carbon atoms to position 17 by preparing the cyanohydrin (XXIX), and were followed independently by A. Butenandt and J. Schmidt-



Thomé.⁵⁷ The cyanohydrin proved to be somewhat difficult to deal with, as it lost the nitrile group readily. The German workers dehydrated the acetate with phosphoryl chloride in pyridine to give the Δ^{16} -unsaturated nitrile (XXX), which was then converted

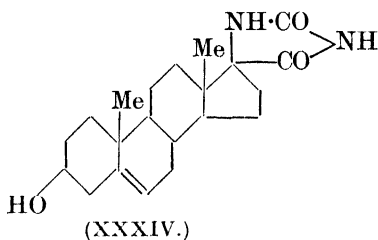
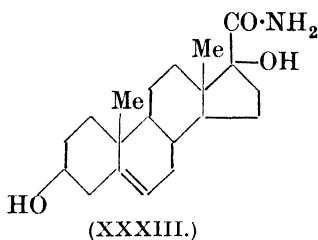
⁵⁶ *J. Pharm. Soc. Japan*, 1937, **57**, 96; 1938, **58**, 116; *Chem. Zentr.*, 1937, II, 1825.

⁵⁷ *Naturwiss.*, 1938, **26**, 253; *Ber.*, 1938, **71**, 1487; cf. J. Schmidt-Thomé, *Angew. Chem.*, 1938, **51**, 494; W. Schoeller and A. Serini (Schering A.-G.), D. R.-P. 657,017.

into the acid (XXXI) by sodium hydroxide at 180° . Reduction with Raney nickel yielded 3(β)-hydroxy- Δ^5 -aetiocholenic acid (XI), an intermediate in the degradation of stigmaterol to progesterone.^{31, 32}

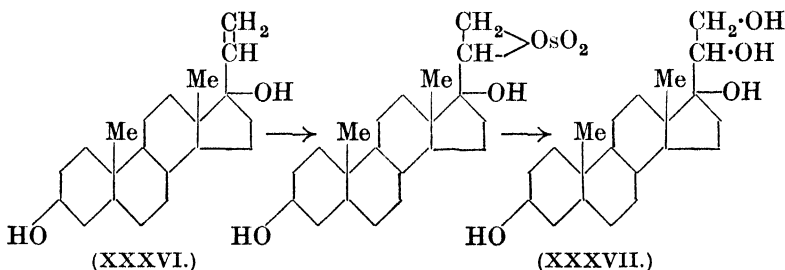
A possible alternative to this path to progesterone, which is a matter of six stages, is provided by the interaction of (XXX) with methylmagnesium iodide to give $\Delta^{5:16}$ -pregnadien-3-ol-20-one (XXXII).

K. Miescher and A. Wettstein,⁵⁸ following the same line, found conditions under which the cyanohydrin diacetate was converted by hydrochloric acid into the amide (XXXIII) and thence into



3(β) : 17-dihydroxy- Δ^5 -aetiocholenic acid (XXIV), identical with the product from 3(β) : 17-dihydroxy-17-ethynyl- Δ^5 -androstene obtained by L. Ruzicka and K. Hofmann.⁴⁶ They also prepared from Δ^5 -androsten-3(β)-ol-20-one acetate the 17-*spirohydantoin* (XXXIV).

A. Serini and W. Logemann⁵⁹ attempted to get an actual compound of the adrenal cortical group from one of the androstane group by oxidation of 3(β) : 17-dihydroxy-17-vinylandrostane (XXXVI) with osmium tetroxide :



The resulting *allopregnane*-3 : 17 : 20 : 21-tetrol (XXXVII), and the Δ^5 -pregnene-3 : 17 : 20 : 21-tetrol and Δ^4 -pregnene-17 : 20 : 21-triol-3-one, prepared by analogous methods, are not, however, likely to be identical with natural adrenal cortical compounds owing to the

⁵⁸ *Helv. Chim. Acta*, 1938, **21**, 1317.

⁵⁹ *Ber.*, 1938, **71**, 1362.

difference of configuration at position 17. This question will be considered at the end of the following section.

Adrenal Steroids.—In the last two years the chemistry of constituents of the adrenal cortex has developed with great rapidity, and the result of the work of E. C. Kendall, T. Reichstein, and O. Wintersteiner and their respective associates has been not merely the isolation of two compounds which possess the characteristic physiological activity of the adrenal cortex in high degree, but also the isolation of a large group of other related compounds of the androstane and pregnane series and the partial or complete elucidation of their constitution. In view of the volume and complexity of this work, it is fortunate that reference can be made to several reviews,⁶⁰ in which accounts are given which are both detailed and consecutive.

The compounds isolated are enumerated in the table, with their provisional designations, and the constitution assigned, with the appropriate references.

The separation of this series of compounds has not only great importance on account of the isolation and consequent determination of the constitution of substances of high hormonal activity but has potential value from the physiological point of view when the problem of the relations of these substances to each other *in vivo* can be attacked. As an example of the separation of a group of natural compounds by methods involving only the gentlest treatment, the work of Reichstein and his collaborators will serve as a model for many other investigations. The highly hydroxylated character of the side-chains in some cases, with the resulting solubility in water, was a factor which enabled separation by processes of partition. The possibility of separation by ketone reagents led to the next step, application of the Girard-Sandulesco reagent T (trimethylcarbohydrazidomethylammonium chloride⁸⁸) to the fractional formation of water-soluble derivatives of the ketonic substances, followed by their fractional decomposition.^{72, 75} Fractionation of hydroxyl compounds or of their acetates by elution of "chromatographic" adsorption columns followed,⁸¹ and, since reducing ketols were separable as acetates, but not recoverable by ordinary methods of hydrolysis, a new technique of hydrolysis by alkali carbonates was elaborated⁸⁹ and applied.^{82, 83}

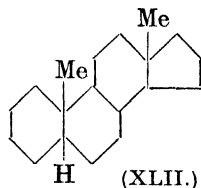
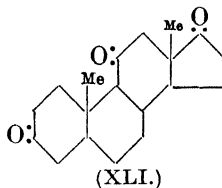
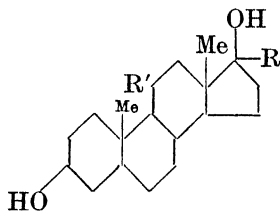
The determination of the constitution of these compounds has proceeded by the steps of showing the presence of the steroid nucleus,

⁶⁰ T. Reichstein, *Ergeb. Vitamin- u. Hormonforsch.*, 1938, **1**, 334; Abderhalden's "Handb. der biol. Arbeitsmet.," 1938, *Abt. V, Teil 3B*, s. 1367; O. Wintersteiner and P. E. Smith, *Ann. Rev. Biochem.*, 1938, **7**, 253; K. Miescher, *Angew. Chem.*, 1938, **51**, 551.

Steroids from the Adrenal Cortex.

Alphabetical and numerical designations given by Kendall <i>et al.</i> (K.), Reichstein <i>et al.</i> (R.), and Winterstein <i>et al.</i> (W.).	Empirical formulæ.	Systematic names.	Isolation.	References.	Constitution.
D (K.); A/1 (R.); A (W.)	C ₂₁ H ₃₄ O ₅	<i>allo</i> Pregnane-3 : 11 : 17 : 20 : 21-pentol	62, 64, 72	70, 74	
C (K.); C/2 (R.); D (W.)	C ₂₁ H ₃₄ O ₅	<i>allo</i> Pregnane-3 : 11 : 17 : 21-tetrol-20-one	61, 62, 68, 72	70	
G (K.); D/3 (R.); ?B (W.)	C ₂₁ H ₃₂ O ₅	<i>allo</i> Pregnane-3 : 17 : 21-triol-11 : 20-dione	68, 72	70	
— ; E/4 (R.); —	C ₂₁ H ₃₂ O ₅	Δ ⁴ -Pregnene-11 : 17 : 20 : 21-tetrol-3-one	72, 78	75, 79	
F (K.); M/5 (R.); —	C ₂₁ H ₃₂ O ₅	Δ ⁴ -Pregnene-11 : 17 : 21-triol-3 : 20-dione	68, 77	70, 78, 79	
E (K.); Fa/6 (R.); F (W.)	C ₂₁ H ₃₀ O ₅	Δ ⁴ -Pregnene-17 : 21-diol-3 : 11 : 20-trione	62, 63, 64, 65, 66, 67, 68, 75	70, 71, 78, 79	
— ; K (R.); —	C ₂₁ H ₃₀ O ₄	<i>allo</i> Pregnane-3 : 17 : 20 : 21-tetrol	81	81	
— ; P (R.); —	C ₂₁ H ₃₄ O ₄	<i>allo</i> Pregnane-3 : 17 : 21-triol-20-one	82	82	
— ; R (R.); —	C ₂₁ H ₃₄ O ₄	<i>allo</i> Pregnane-3 : 11 : 21-triol-20-one	83	86	
?B (K.); N/8 (R.); —	C ₂₁ H ₃₀ O ₄	<i>allo</i> Pregnane-3 : 21-diol-11 : 20-dione	69, 81	69, 82	
B (K.); H/7 (R.); —	C ₂₁ H ₃₀ O ₄	Δ ⁴ -Pregnene-11 : 21-diol-3 : 20-dione (Corticosterone)	64, 66, 76, 77	69, 75, 80	
— ; S (R.); —	C ₂₁ H ₃₀ O ₄	Δ ⁴ -Pregnene-17 : 21-diol-3 : 20-dione	83	86	
A (K.); —/8 (R.); —	C ₂₁ H ₂₈ O ₄	Δ ⁴ -Pregnen-21-ol-3 : 11 : 20-trione	64	66, 69, 78	
— ; J & O (R.); —	C ₂₁ H ₃₆ O ₃	<i>allo</i> Pregnane-3 : 17 : 20-triols (stereoisomerides)	75, 81	81	
— ; L (R.); G (W.)	C ₂₁ H ₃₄ O ₃	<i>allo</i> Pregnane-3 : 17-diol-20-one	75	87	
— ; Q (R.); —	C ₂₁ H ₃₀ O ₃	Δ ⁴ -Pregnen-21-ol-3 : 20-dione (Deoxycorticosterone)	83	84	
—	C ₂₁ H ₃₄ O ₂	<i>allo</i> Pregnan-3-ol-20-one	85		
—	C ₂₁ H ₃₄ O ₂	Δ ⁴ -Pregnene-3 : 20-dione (Progesterone)	85		
—	C ₁₉ H ₂₆ O ₂	Androstane-3(β) : 11-diol-17-one	83	83	
— ; G (R.); —	C ₁₉ H ₂₄ O ₃	Δ ⁴ -Androstene-3 : 11 : 17-trione (Adrenosterone)	72, 73	72, 73	

followed by clearing up the nature of the side-chain, recognition of the pregnane skeleton, and provisional allocation to position 11 of the relatively inert hydroxyl or ketone group which some of



[XXXVIII; $R = CH(OH) \cdot CH_2 \cdot OH$, $R' = OH$]
 (XXXIX; $R = CO \cdot CH_2 \cdot OH$, $R' = OH$)
 (XL; $R = CO \cdot CH_2 \cdot OH$, $R' = :O$)

them possess. The first three substances in the table (XXXVIII, XXXIX, XL) are oxidised by chromium trioxide to give a saturated

⁶¹ O. Wintersteiner and J. J. Pfiffner, *J. Biol. Chem.*, 1935, **109**, *Sci. Proc.*, **29**, c. ⁶² *Idem, ibid.*, 1935, **111**, 599.

⁶³ *Idem, ibid.*, 1936, **114**, *Sci. Proc.*, **30**, lxxx; *ibid.*, 1936, **116**, 291; E. C. Kendall, H. L. Mason, C. S. Myers, and W. D. Allers, *ibid.*, **114**, *Sci. Proc.*, **30**, lvii.

⁶⁴ H. L. Mason, C. S. Myers, and E. C. Kendall, *ibid.*, 1936, **114**, 613.

⁶⁵ *Idem, Proc. Staff Meetings Mayo Clinic*, 1936, **11**, 351; *J. Biol. Chem.*, 1936, **116**, 267.

⁶⁶ E. C. Kendall, H. L. Mason, W. H. Hoehn, and B. F. McKenzie, *Proc. Staff Meetings Mayo Clinic*, 1937, **12**, 136.

⁶⁷ *Idem, ibid.*, 1937, **12**, 270.

⁶⁸ *Idem, J. Biol. Chem.*, 1937, **119**, *Sci. Proc.*, **31**, lvi.

⁶⁹ H. L. Mason, W. M. Hoehn, B. F. McKenzie, and E. C. Kendall, *ibid.*, 1937, **120**, 719.

⁷⁰ H. L. Mason, W. M. Hoehn, and E. C. Kendall, *ibid.*, 1938, **124**, 459.

⁷¹ H. L. Mason, *ibid.*, p. 475.

⁷² T. Reichstein, *Helv. Chim. Acta*, 1936, **19**, 29.

⁷³ *Idem, ibid.*, p. 223.

⁷⁴ *Idem, ibid.*, p. 402.

⁷⁵ *Idem, ibid.*, p. 1107.

⁷⁶ T. Reichstein, E. Laqueur, I. E. Uyldert, P. de Fremery, and R. W. Spanhoff, *Proc. K. Akad. Wetensch. Amsterdam*, 1936, **39**, 10.

⁷⁷ P. de Fremery, E. Laqueur, T. Reichstein, R. W. Spanhoff, and I. E. Uyldert, *Nature*, 1937, **139**, 26.

⁷⁸ T. Reichstein, *Helv. Chim. Acta*, 1937, **20**, 953.

⁷⁹ *Idem, ibid.*, p. 978.

⁸⁰ M. Steiger and T. Reichstein, *Nature*, 1938, **141**, 202; *Helv. Chim. Acta*, 1938, **21**, 161.

⁸¹ *Idem, ibid.*, p. 546.

⁸² T. Reichstein and T. Gätzi, *ibid.*, p. 1185.

⁸³ T. Reichstein and J. v. Euw, *ibid.*, p. 1197.

⁸⁴ M. Steiger and T. Reichstein, *Nature*, 1937, **139**, 925.

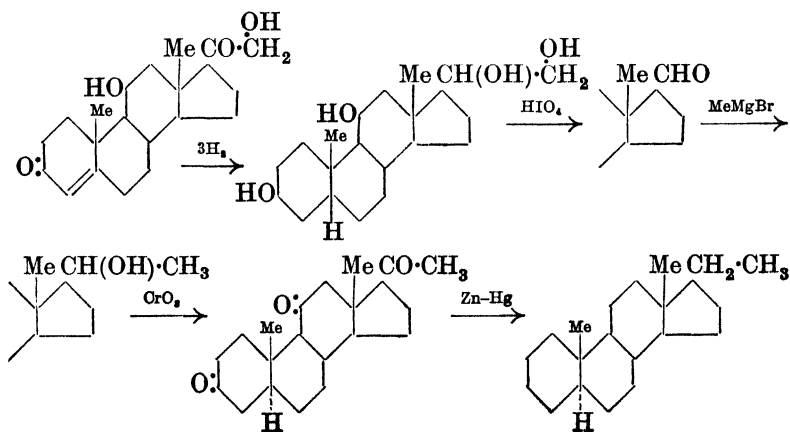
⁸⁵ D. Beall and T. Reichstein, *ibid.*, 1938, **142**, 479; D. Beall, *Biochem. J.*, 1938, **32**, 1957.

⁸⁶ T. Reichstein, *Helv. Chim. Acta*, 1938, **21**, 1490.

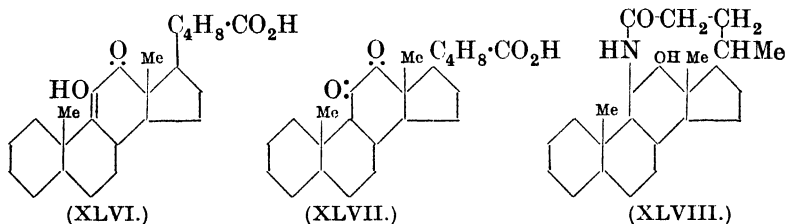
⁸⁷ T. Reichstein and K. Gätzi, *ibid.*, p. 1497.

⁸⁸ A. Girard and G. Sandulesco, *ibid.*, 1936, **19**, 1095.

⁸⁹ T. Reichstein and J. v. Euw, *ibid.*, 1938, **21**, 1181.



11-Substituted derivatives. The "inert," third oxygen atom of the adrenal steroids, in view of the fact that no α - or β -diketo-compounds have been obtained, might be in position 6, 7, 11, or 12. The supposedly "inert" positions 11 and 12 have been favoured, but 6 and 7 are not rigidly excluded. Since position 12 has been dismissed,⁶⁷ position 11 has been provisionally accepted by all the workers concerned, pending some direct proof. Unreactive hydroxylic or ketonic groups have been found in other natural steroids, and by a process of elimination or other type of indirect evidence, position 11 has been assigned to this substituent, *e.g.*, in digoxigenin,⁹⁰ the stereoisomeric sarmentogenin,⁹¹ and uranetriol⁹² from the urine of pregnant mares. Attempts to prepare reference compounds with 11-substitution have been made from several directions. R. E. Marker and E. J. Lawson⁹³ reported the preparation of 3 : 11-dihydroxy-12-ketocholanic acid by bromination and hydrolysis of 12-keto-3-acetoxycholanic acid, but failed to isolate a product of reduction of the 12-keto-group. J. Barnett and T. Reichstein⁹⁴ pursued a somewhat similar course in preparing the isomeric 11-hydroxy-12-ketocholanic acids; they described the interesting properties of the 11 : 12-diketo-acid, which has stable the enolic (XLVI) and ketonic (XLVII) forms, and obtained a compound which they formulated as (XLVIII) by Raney reduction of the ester monoxime, but failed to attain the desired 11-derivative.



M. Steiger and T. Reichstein⁹⁵ proceeded to test the assumption that digoxigenin and corticosterone both contained 11-hydroxyl groups by attempting to degrade both compounds to aetiocholanic acids with substituents in positions 3 and 11. The two series of products proved to be different, and it was concluded that in one series the assumed constitution must be incorrect. W. M. Hoehn and H. L. Mason⁹⁶ prepared authentic aetiocholanic acid derivatives

⁹⁰ R. Tschesche and K. Bohle (with H. Grasshof), *Ber.*, 1936, **69**, 793.

⁹¹ R. Tschesche and K. Bohle, *ibid.*, p. 2497.

⁹² R. E. Marker, O. Kamm, T. S. Oakwood, E. L. Wittle, and E. J. Lawson, *J. Amer. Chem. Soc.*, 1938, **60**, 1061.

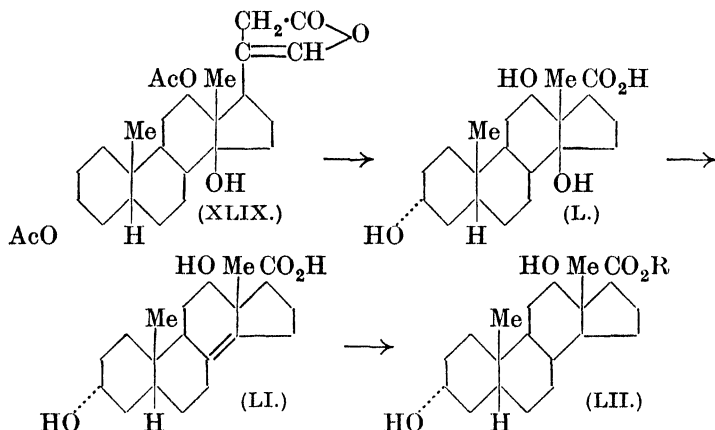
⁹³ *Ibid.*, p. 1334.

⁹⁴ *Helv. Chim. Acta*, 1938, **21**, 926.

⁹⁵ *Ibid.*, p. 828.

⁹⁶ *J. Amer. Chem. Soc.*, 1938, **60**, 1493, 2566.

with hydroxyl or carbonyl in positions 3 and 12 from deoxycholic acid, and these were found⁹⁷ to be identical with products from digoxigenin. The assumed constitution of adrenal steroids remains, at least, unassailed, but the formulæ of digoxigenin and sarmentogenin require revision. The method of degradation of digoxigenin devised by M. Steiger and T. Reichstein may be expected to give valuable information when applied to other heart poisons. It consists of permanganate oxidation of the diacetate (XLIX), followed by elimination of the tertiary hydroxyl group, and reduction of the double linking by Raney nickel, to give 3:12-dihydroxyaetiocholic acid as shown in formulæ (XLIX) to (LII). A process of oxidation, bromination, debromination to the 3-keto- Δ^4 -acid, and reduction yielded the corresponding aetioallocholic acid.



Configuration at C₁₇. A further problem remaining to be settled in the adrenal steroid group is that of the configuration at C₁₇. This is part of a general problem which arose in a comparatively short period in connexion with all three groups of sex hormones. *allo*Pregnan-3(β)-ol-20-one⁹⁸ and Δ^5 -pregnen-3(β)-ol-20-one⁹⁹ were shown to be converted by alkali into "iso"-compounds, the formation of which was explained by alteration of the configuration at C₁₇. The latter had considerably decreased dextrorotation, and no longer gave insoluble digitonides. The isomeric oestradiols¹ showed analogous differences, and isomeric dihydroequilenins² were

⁹⁷ H. L. Mason and W. M. Hoehn, *J. Amer. Chem. Soc.*, 1938, **60**, 2824.

⁹⁸ A. Butenandt and L. Mamoli, *Ber.*, 1935, **68**, 1845.

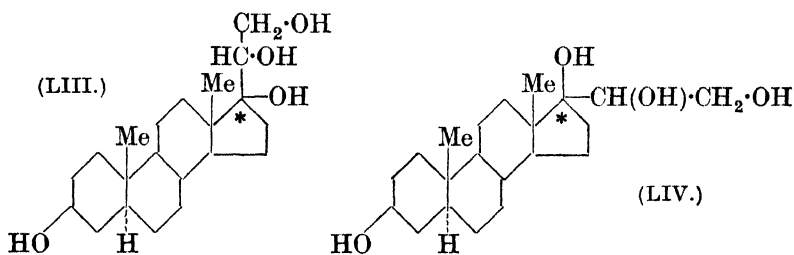
⁹⁹ A. Butenandt and G. Fleischer, *Ber.*, 1937, **70**, 96.

¹ *Ann. Reports*, 1936, **33**, 361; O. Wintersteiner, *J. Amer. Chem. Soc.*, 1937, **59**, 765; A. Butenandt and C. Goergens, *Z. physiol. Chem.*, 1937, **248**, 129.

² R. E. Marker, O. Kamm, T. S. Oakwood, and F. H. Tendick, *J. Amer. Chem. Soc.*, 1937, **59**, 768; R. E. Marker, *ibid.*, 1938, **60**, 1897.

prepared. Isomeric androstane-3(α) : 17-diols were separated,³ and the isomeride formed in greater amount by reduction of androsterone was allotted, on the basis of superior reactivity,⁴ the configuration with the 17-hydroxyl and the 13-methyl group *trans* to each other.

The interesting possibility of correlating digitonide formation, relative dextrorotation, and higher physiological activity has been discussed,⁵ but the position is still obscure and awaits systematic investigation. As far as concerns products obtained by addition of hydrogen cyanide, acetylene, or alkylmagnesium halides to the keto-group in position 17, there is evidence from identity of transformation products and of colour reactions⁶ that they belong to the same group with *trans*-configuration. In particular, T. Reichstein and K. Gätzi⁷ point out that all the pregnane derivatives obtained by interaction of acetylene or ethylmagnesium halides with androstan-3(β)-ol-17-one or Δ^5 -androsten-3(β)-ol-17-one can be reduced to the same *allopregnane*-3 : 17-diol. These, which compose what they call the 17(α)-series, are not precipitated by digitonin, but the natural adrenal steroids with 3(β)- and 17-hydroxyl groups are precipitated by digitonin and belong to the 17(β)-series. It does not seem clear at the moment whether α - α estradiol (higher dextrorotation and physiological activity, precipitable by digitonin, principal natural product) is a 17(β)- or a 17(α)-hydroxy-compound, and it affords a good example of the uncertainties in configurational relations which remain to be made clear. In the meantime, an explanation is afforded for the difference of the synthetic⁸ and the natural⁷ *allopregnane*-3(β) : 17 : 20 : 21-tetrol, which are respectively 17(α)- and 17(β)-hydroxy-compounds, and are conventionally represented as (LIII) and (LIV).



³ L. Ruzicka and H. Kägei, *Helv. Chim. Acta*, 1936, **19**, 842.

⁴ L. Ruzicka and M. W. Goldberg, *ibid.*, p. 99; L. Ruzicka and H. Kägei, *ibid.*, 1937, **20**, 1557.

⁵ O. Wintersteiner, *Cold Spring Harbor Symposia on Quantitative Biology*, 1937, **5**, 25.

⁶ K. Miescher and A. Wettstein, *Helv. Chim. Acta*, 1938, **21**, 1317; H. Kägei and K. Miescher, *Chem. and Ind.*, 1938, **57**, 276; cf. L. Ruzicka, K. Hofmann, and H. F. Meldahl, *Helv. Chim. Acta*, 1938, **21**, 597.

⁷ *Ibid.*, p. 1185.

⁸ A. Serini and W. Logemann, *Ber.*, 1938, **71**, 1362.

Urinary Steroids.—The possibility of a connexion between steroids present in the adrenal cortex and certain of those excreted in the urine was discussed in the last Report,⁹ and is now more firmly established, at least in the case of certain abnormal conditions.¹⁰ The isolation of androsterone and Δ^5 -androsten-3(β)-ol-17-one from the urine of normal women¹¹ and of androsterone from the urine of pregnant women¹² shows that these compounds are at least not specific to the male organism, but leaves open the question whether they are derived from the adrenal cortical secretion. G. C. Butler and G. F. Marrian¹³ suggest that the pregnane-3(α):17:20-triol isolated by them from a pathological urine may be the intermediate stage in a breakdown to the aetiocholan-3(α)-ol-17-one present in the same urine and typify the *in vivo* degradation of steroids of the pregnane or *allopregnane* series to those of the aetiocholane or androstane series, respectively, beginning with the introduction of the tertiary hydroxyl group in position 17.

The investigations of R. E. Marker and his co-workers into the steroids of urine, carried out with large amounts of material, have led to the isolation of a series of pregnane derivatives which may be looked upon as excretory transformation products of the steroids of the *corpus luteum* of the ovary, and of the adrenal cortex. From the urine of pregnant mares there have been obtained pregnanediol,¹⁴ *allopregnanediol*,¹⁴ pregnanediolone, *allopregnanediolone*, *allopregnan-3-ol-20-one*, *uran-11-ol-3-one*,¹⁵ *urane-3:11-diol*,¹⁶ Δ^4 -pregnenediol,¹⁷ *pregnanetriol-A*¹⁸ (later named *uranetriol*¹⁹), *pregnanetriol-B*, and (?) *allopregnane-3(β):11:20:21-tetrol*.²⁰ *Pregnanetriol-B*, originally isolated by G. F. Marrian and his co-workers,²¹ was

⁹ *Ann. Reports*, 1936, **33**, 360.

¹⁰ Cf. the discussion by R. K. Callow, *Proc. Roy. Soc. Med.*, 1938, **31**, 841.

¹¹ (Mrs.) N. H. Callow and R. K. Callow, *Biochem. J.*, 1938, **32**, 1759.

¹² R. E. Marker and E. J. Lawson, *J. Amer. Chem. Soc.*, 1938, **60**, 2928.

¹³ *J. Biol. Chem.*, 1938, **124**, 237; *Nature*, 1938, **142**, 400.

¹⁴ R. E. Marker, O. Kamm, H. M. Crooks, T. S. Oakwood, E. J. Lawson, and E. L. Wittle, *J. Amer. Chem. Soc.*, 1937, **59**, 2297. For a review of the natural and the synthetic pregnanediols and pregnanolones, cf. R. E. Marker, O. Kamm, E. L. Wittle, T. S. Oakwood, E. J. Lawson, and J. F. Laucius, *ibid.*, p. 2291.

¹⁵ R. E. Marker, E. J. Lawson, E. L. Wittle, and H. M. Crooks, *ibid.*, 1938, **60**, 1559.

¹⁶ R. E. Marker, E. Rohrmann, and E. L. Wittle, *ibid.*, p. 1561.

¹⁷ R. E. Marker and E. Rohrmann, *ibid.*, p. 1565.

¹⁸ R. E. Marker, O. Kamm, H. M. Crooks, T. S. Oakwood, E. L. Wittle, and E. J. Lawson, *ibid.*, p. 210.

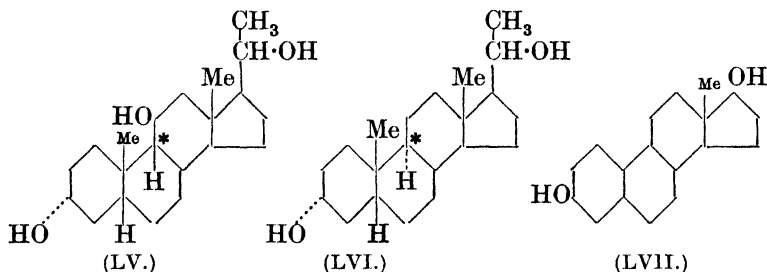
¹⁹ R. E. Marker, O. Kamm, E. L. Wittle, and E. J. Lawson, *ibid.*, p. 1061.

²⁰ R. E. Marker, E. J. Lawson, E. Rohrmann, and E. L. Wittle, *ibid.*, p. 1555.

²¹ E. R. Smith, D. Hughes, G. F. Marrian, and G. A. D. Haslewood, *Nature*, 1933, **132**, 102; G. A. D. Haslewood, G. F. Marrian, and E. R. Smith, *Biochem. J.*, 1934, **28**, 1316.

assigned²² the constitution of pregnane-3(α):4:20-triol. A. D. Odell and G. F. Marrian²³ have since obtained evidence against this formulation, and propose instead pregnane- or *allopreg*nane-3(α):6:20-triol.

The "urane" derivatives have been assigned¹⁹ a structure which is stereoisomeric with that of the pregnane derivatives in virtue of a difference in orientation at C₉, and uranetriol and pregnanediol are formulated as (LV) and (LVI), respectively. A number



of derivatives have been prepared,^{19,24} including the parent hydrocarbon, but since the proposed structure was based very largely on analogy with assumed structures of sarmentogenin and digoxigenin which are no longer tenable^{95,97} (cf. p. 298), it seems justifiable to delay reporting further on this work until controversial points are settled.

Pregnane-3(α):20(α)-diol, *allopreg*nane-3(α):20(α)-diol, and *allopreg*nane-3(β):20(α)-diol have been isolated from bull's urine.²⁵

The urine of pregnant women yielded *allopreg*nan-3(α)-ol-20-one,²⁶ pregnan-3(α)-ol-20-one,²⁷ and pregnan-3(α)-ol.¹² The first-named compound was styled the androgenic principle of human pregnancy urine,²⁸ but A. Butenandt and A. Heusner²⁹ find that it has no androgenic activity.

R. E. Marker and his co-workers³⁰ have further isolated two

²² R. E. Marker, O. Kamm, E. L. Wittle, T. S. Oakwood, and E. J. Lawson, *J. Amer. Chem. Soc.*, 1938, **60**, 1067.

²³ *J. Biol. Chem.*, 1938, **125**, 333.

²⁴ R. E. Marker, E. L. Wittle, and T. S. Oakwood, *J. Amer. Chem. Soc.*, 1938, **60**, 1567.

²⁵ R. E. Marker, E. L. Wittle, and E. J. Lawson, *ibid.*, p. 2931.

²⁶ R. E. Marker, O. Kamm, and R. V. McGrew, *ibid.*, 1937, **59**, 616.

²⁷ R. E. Marker and O. Kamm, *ibid.*, p. 1373.

²⁸ R. E. Marker, O. Kamm, D. M. Jones, E. L. Wittle, T. S. Oakwood, and H. M. Crooks, *ibid.*, p. 768.

²⁹ *Angew. Chem.*, 1938, **51**, 493; *Z. physiol. Chem.*, 1938, **256**, 236.

³⁰ R. E. Marker, E. Rohrmann, E. L. Wittle, and E. J. Lawson, *J. Amer. Chem. Soc.*, 1938, **60**, 1512; R. E. Marker, E. Rohrmann, E. J. Lawson, and E. L. Wittle, *ibid.*, p. 1901; R. E. Marker and E. Rohrmann, *ibid.*, p. 2927.

isomeric hexahydroœstradiols (LVII), œstranediol-A and œstranediol-B from the urine of non-pregnant women. The second of these compounds is identical with a reduction product of œstrone,³¹ and has the same configuration at C₁₇ as α -œstradiol.

A new excretory product of the male hormone group detected in extracts of men's urine is aetiocholane-3(α):17-diol,³² but the circumstances in which it was isolated compel the reservation that it may not exist in the urine as such, but be formed during subsequent treatment.

In a highly ingenious but speculative paper based on the chemical work reported in papers on steroids in urine and tissues, thirty-nine of which are from his own laboratory, R. E. Marker³³ produces a general scheme for the metabolism of the steroidal hormones in the body. The schemes of biogenesis of steroids of simpler type from cholesterol are shown to be open to serious objections, as, for instance, the difficulty of removing the side-chain from position 17 except by the most violent methods, and the difficulty of introducing a hydroxyl group into the 11-position postulated for the inert oxygen of the adrenal cortical group and certain urane compounds. A scheme for the biological reduction of progesterone has been constructed on the assumption that two types of change take place: (a) reduction of the 4:5-double linking to give either *cis*- or *trans*-derivatives (coprostane or cholestane type), followed by reduction of the 3-carbonyl group to give 3(α)-hydroxy-compounds, and (b) the reduction of the Δ^4 -3-keto-grouping successively to Δ^5 -3(β)-hydroxy- (cholesterol type) and 3(β)-*trans*-derivatives (cholestanol type). So far, generalisation and experimental facts correspond, for the compounds isolated fit in, and only two hypothetical products are included. Extension of the same generalisation to the male hormone group, however, entails the assumption that Δ^4 -androstene-3:17-dione is the original hormone, and eight out of twelve compounds in the resulting scheme have not been isolated from either gland or urine.

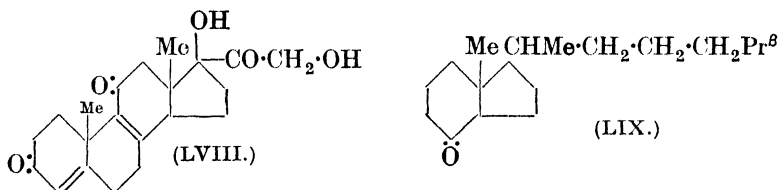
These speculations become entirely independent of experimental facts when Δ^4 :⁸-pregnadiene-17:21-diol-3:11:20-trione (LVIII) is proposed as the hypothetical common precursor of the C₁₈, C₁₉, and C₂₁ sex hormones and the adrenal cortical steroids. The justification of these adventurous hypotheses not only by isolation of further substances from natural sources and by synthetical work, but also by observations of a more physiological type, will be awaited with interest.

³¹ W. Dirscherl, *Z. physiol. Chem.*, 1936, **239**, 53.

³² A. Butenandt, K. Tscherning, and H. Dannenberg, *ibid.*, 1937, **248**, 205.

³³ *J. Amer. Chem. Soc.*, 1938, **60**, 1725.

The Vitamins-D and their Precursors.—Further work has been carried out on the occurrence and composition of natural provitamins-D; so far, only two compounds have been found,



7-dehydrocholesterol ($\Delta^5:7$ -cholestadien-3-ol) in pig's skin³⁴ and in the common whelk,³⁵ and ergosterol in other invertebrates³⁵ and in wheat-germ oil.³⁶ 7-Dehydro-sitosterol and -stigmasterol were not found. Further $\Delta^5:7$ -steroids which are potential provitamins have been prepared. G. A. D. Haslewood³⁷ obtained 3(β)-hydroxy- $\Delta^5:7$ -choladienic acid from methyl 3:7-dibenzoyloxy- Δ^5 -cholenate by the action of dimethylaniline, a method which is superior to the pyrolytic one previously used for introducing the C₇₋₈ double bond. $\Delta^5:7$ -Androstadiene-3(β):17-diol, obtained by analogous methods,³⁸ is a potentially interesting compound, not only from the physiological point of view, but also in view of the possible preparation of a "vitamin-D" perhaps more amenable to physical methods in determination of its structure than the compounds with long side-chains in position 17.

Vitamin-D₃ has been obtained crystalline from tunny-liver oil, and the presence of a small amount of admixed calciferol has been recognised.³⁹ Halibut-liver oil also contains vitamin-D₃.⁴⁰

Synthetic vitamin-D₃ has been crystallised,⁴¹ and a detailed study of the irradiation products of 7-dehydrocholesterol⁴² has led to the isolation of lumisterol-3 and tachysterol-3, analogous to the products from ergosterol. Ozonisation of vitamin-D₃ yielded a ketone, probably (LIX), in complete analogy with calciferol. "Vitamin-D₄" (from irradiation of 22:23-dihydroergosterol) has been isolated and characterised.⁴³

³⁴ A. Windaus and F. Bock, *Z. physiol. Chem.*, 1937, **245**, 168.

³⁵ F. Bock and F. Wetter, *ibid.*, 1938, **256**, 33.

³⁶ A. Windaus and F. Bock, *ibid.*, p. 47.

³⁷ J., 1938, 224.

³⁸ A. Butenandt, E. Hausmann, and J. Paland (with, in part, D. von Dresler and U. Meinerts), *Ber.*, 1938, **71**, 1316.

³⁹ H. Brockmann and A. Busse, *Naturwiss.*, 1938, **26**, 122; *Z. physiol. Chem.*, 1938, **256**, 252.

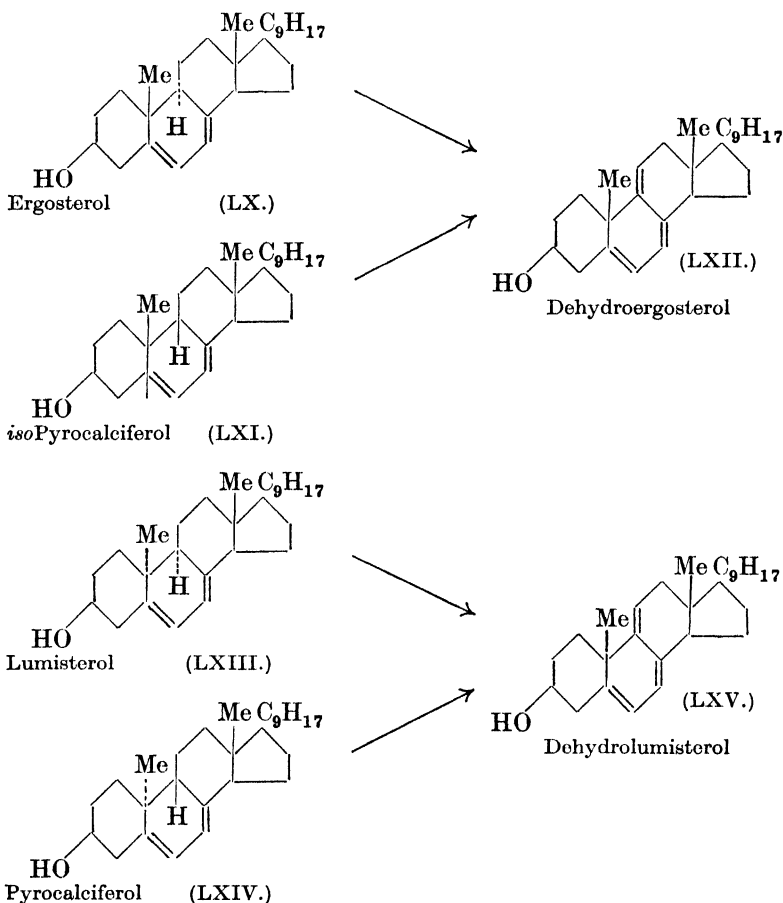
⁴⁰ H. Brockmann, *Z. physiol. Chem.*, 1937, **245**, 96.

⁴¹ F. Schenck, *Naturwiss.*, 1937, **25**, 159.

⁴² A. Windaus, M. Deppe, and W. Wunderlich, *Annalen*, 1937, **533**, 118.

⁴³ A. Windaus and G. Trautmann, *Z. physiol. Chem.*, 1937, **247**, 185.

The flat contradiction between the conclusions of X-ray crystallography and of chemistry as to the structure of calciferol still remains unresolved. K. v. Auwers,⁴⁴ however, considers that measurements of n and dispersive power are concordant with the Windaus formula, rather than with a 4-ring structure. An examination of the physical



constants of calciferol in a large series of samples⁴⁵ showed a variation in the optical rotation which was relatively greater than that of the ultra-violet absorption: the significance of this is not understood. Further work on lumisterol confirms the hypothesis that it differs from ergosterol simply in the steric position of the 10-methyl

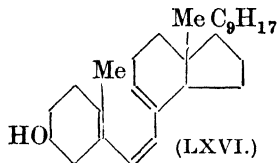
⁴⁴ *Annalen*, 1938, **533**, 255.

⁴⁵ F. W. Anderson, A. L. Bacharach, and E. L. Smith, *Analyst*, 1937, **62**, 430.

group, as postulated by K. Dimroth⁴⁶ and by A. Windaus and K. Dimroth.⁴⁷ These authors, finding that ergosterol (LX) and isopyrocalciferol (LXI) yielded the same dehydroergosterol (LXII), whilst lumisterol (LXIII) and pyrocalciferol (LXIV) yielded the same dehydrolumisterol (LXV), proposed a scheme which may be represented as on p. 304.

An alternative scheme, according to which the relations might be explained by variation of orientation round C_3 and C_9 , instead of round C_9 and C_{10} , was shown⁴⁸ to be impossible, on account of the non-identity of *epi*ergosterol with either lumisterol or pyrocalciferol and of *epi*lumisterol with either ergosterol or isopyrocalciferol. The results of comparative studies of analogous ergosterol and lumisterol derivatives by chemical and ultra-violet spectrographic methods⁴⁹ are concordant with these conclusions.

The constitution of tachysterol has been discussed by W. Grundmann,⁵⁰ who considers that the possibility



of its being a stereoisomeride of calciferol can be ruled out. The evidence so far obtained from ozonolysis of adducts with citraconic anhydride⁵¹ or with methyl acetylenedicarboxylate, or from direct oxidative degradation, suggests the

$\Delta^{5(10):6:8}$ -structure (LXVI) rather than the $\Delta^{1(10):5:7}$ -structure previously discussed.

A. Windaus and K. Buchholz⁵² have oxidised calciferol by Oppenauer's method to the corresponding ketone. This has not been obtained crystalline, but it has the same absorption spectrum as calciferol: its antirachitic activity is 1/300 of that of calciferol.

An interesting side-line to the calciferol problem is the behaviour of pyrocalciferol and isopyrocalciferol on irradiation.⁵³ These appear to be transformed directly into well-characterised compounds, photopyrocalciferol and photoisopyrocalciferol, which contain double linkings that are not conjugated but are probably in the 4:5- and 7:8-positions. The reactions are reversed on heating.

The occurrence of photochemical change in steroids containing conjugated double linkings not in the "provitamin" or 5:7-position is a new development. $\Delta^{6:8}$ -Cholestadien-3-ol, obtained as a by-

⁴⁶ *Ber.*, 1936, **69**, 1123.

⁴⁷ *Ibid.*, 1937, **70**, 376.

⁴⁸ I. M. Heilbron, T. Kennedy, F. S. Spring, and G. Swain, *J.*, 1938, 869.

⁴⁹ A. Burawoy, *J.*, 1937, 409; I. M. Heilbron, G. L. Moffet, and F. S. Spring, *ibid.*, p. 411.

⁵⁰ *Z. physiol. Chem.*, 1938, **252**, 151.

⁵¹ Laucht, *Dissert.*, Göttingen, 1936, quoted by W. Grundmann, *loc. cit.*

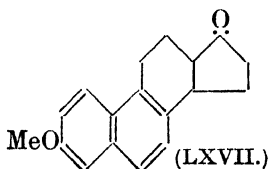
⁵² *Z. physiol. Chem.*, 1938, **256**, 273.

⁵³ K. Dimroth, *Ber.*, 1937, **70**, 1631.

product in the preparation of $\Delta^{5:7}$ -cholestadien-3-ol,⁵⁴ is converted⁵⁵ by ultra-violet irradiation into $\Delta^{6:8}$ -coprostadien-3-ol by a change of configuration on C₅. This is regarded as completely analogous to the change of configuration on C₁₀ in $\Delta^{5:7}$ -compounds, for in each case the primary change is in a position "loosened" by the conjugated system. The two $\Delta^{6:8}$ -compounds and the $\Delta^{5:7}$ -compound give the same "pinacol" on insolation in alcohol containing eosin, and this is confirmed by preparation of the same norsterol (ring II aromatic) by distillation of the pinacol from all three sources. Other transformation products of the stereoisomeric $\Delta^{6:8}$ -compounds are analogous, *e.g.*, the maleic acid adducts, the Δ^8 -3 : 6 : 7-triols, dihydro-derivatives— α -(Δ^8 ,¹⁴) and δ -(Δ^8 ,⁹)—and a "dienol-B₃" (Δ^7 :¹⁴) compound.

A photochemical reaction commonly regarded as characteristic of $\Delta^{5:7}$ -compounds, the formation of a peroxide on irradiation in alcohol containing eosin in presence of oxygen, has been found to occur with $\Delta^{2:4}$ -cholestadiene, which is obtained by dehydration of cholesterol with alumina under special conditions.⁵⁶ The initial disagreement as to the properties of the compound formed has been explained in a somewhat unexpected way by the observation⁵⁷ that the product obtained by irradiation with a tungsten-filament lamp is isomerised by exposure to sunlight. The first product is shown⁵⁷ to be Δ^3 -cholestene 2 : 5-peroxide, since the properties of the product of hydrogenation indicate that it must be cholestane-2 : 5-diol.

Synthesis of Steroids.—Although this Report has dealt only with natural products and the relations between them, it should be mentioned that there has been increasing activity in the exploration of routes to the synthesis of natural steroids.



It seems likely that the next major advance in the chemistry of the steroids will be in this direction. This work has not yet reached a stage at which it could usefully be reported in detail, but an exception may be made in referring to the recent synthesis⁵⁸

of a compound closely related to œstrone, namely, *x*-norequiulinin methyl ether (LXVII), obtained from the product of cyclising 3- β -naphthylcyclopentan-1-one-2-acetic acid.

R. K. C.

⁵⁴ A. Windaus, O. Linsert, and H. J. Eckhardt, *Annalen*, 1938, **534**, 22.

⁵⁵ A. Windaus and G. Zühlsdorff, *ibid.*, 1938, **536**, 204.

⁵⁶ H. E. Stavely and W. Bergmann, *J. Org. Chem.*, 1937, **1**, 575; E. L. Skau and W. Bergmann, *J. Amer. Chem. Soc.*, 1938, **60**, 986; A. Butenandt and H. Kudssus, *Z. physiol. Chem.*, 1938, **253**, 1, 224.

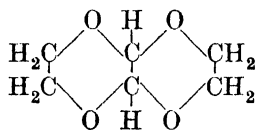
⁵⁷ E. L. Skau and W. Bergmann, *J. Org. Chem.*, 1938, **3**, 166.

⁵⁸ A. Koebner and R. Robinson, *J.*, 1938, 1994.

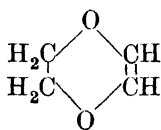
7. HETEROCYCLIC COMPOUNDS.

(a) *Oxygen Ring Compounds.*

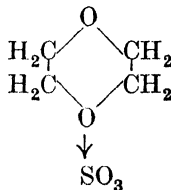
Dioxan Derivatives.—Dioxan (diethylene dioxide), prepared from ethylene glycol¹ and $\beta\beta'$ -dichlorodiethyl ether² by the action of sulphuric acid and alkali respectively, is a useful solvent for cryoscopic and ebullioscopic work, and on account of its miscibility with water and stability towards acids, alkalis and oxidising agents, it provides a suitable medium for many organic reactions. 2:3-Dichlorodioxan, obtained together with smaller amounts of tetra- and hexa-chloro-derivatives by direct chlorination,³ is hydrolysed by the action of warm water to glycol and glyoxal, and the hydrolysate may be used as a convenient source of the latter.^{3,4} The chlorine atoms of the dichloro-derivative are replaceable by alkoxy-groups, and it reacts with glycols and catechol derivatives to give dicyclic compounds such as (I).^{3,5} This compound (I) occurs in *cis*- and *trans*-forms, which have been oriented by measurement of



(I.)



(II.)



(III.)

the dipole moments.⁶ 2:3-Dichlorodioxan reacts with Grignard reagents to give 2:3-dialkyl or -diaryl derivatives,^{5,7} but under certain conditions methylmagnesium iodide yields dioxen (II), from which 2-phenyldioxan may be prepared by addition of hydrogen chloride and subsequent treatment of the unstable 2-chlorodioxan with phenylmagnesium bromide.⁸ Dioxan readily forms double compounds, and recently⁹ the solid product (III) has been prepared by treatment with sulphur trioxide in carbon tetrachloride solution.

¹ L. Anschutz and W. Brocker, *Ber.*, 1926, **59**, 2844; K. Hess and H. Frahm, *ibid.*, 1938, **71**, 2627; U.S.P. 1,681,861.

² B.P. 363,895.

³ J. Böseken, F. Tellegen, and P. C. Henriquez, *Rec. Trav. chim.*, 1931, **50**, 909.

⁴ C. L. Butler and L. N. Critcher, *J. Amer. Chem. Soc.*, 1932, **54**, 2987.

⁵ R. K. Summerbell and R. Christ, *ibid.*, p. 3778.

⁶ J. Böseken, F. Tellegen, and P. C. Henriquez, *Rec. Trav. chim.*, 1935, **54**, 733.

⁷ R. K. Summerbell and R. Christ, *J. Amer. Chem. Soc.*, 1933, **55**, 4547;

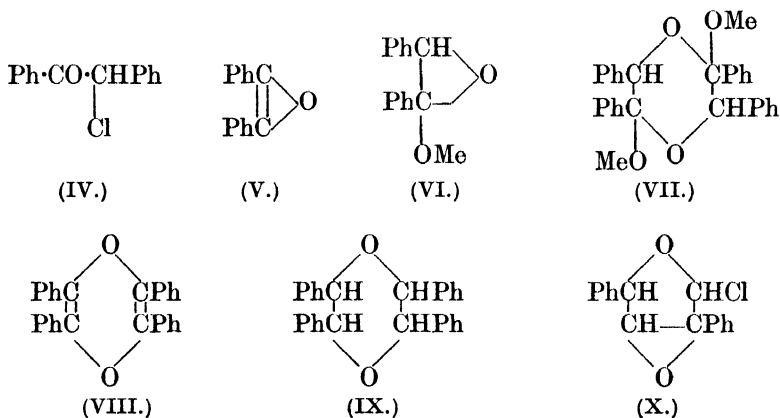
R. K. Summerbell and L. N. Bauer, *ibid.*, 1936, **58**, 759.

⁸ R. K. Summerbell and L. N. Bauer, *ibid.*, 1935, **57**, 2364.

⁹ C. M. Suter, P. B. Evans, and J. M. Keifer, *ibid.*, 1938, **60**, 538.

The product (III) is a more vigorous sulphonating and sulphurating agent than the corresponding pyridine-sulphur trioxide adduct. Benzene, naphthalene and anisole are sulphonated with increasing facility at the ordinary temperature, phenol and aniline give *O*- and *N*-sulphonates respectively, alcohols yield alkyl hydrogen sulphates, and ethylenes are converted into the corresponding carbyl sulphates.

More complicated dioxan derivatives have been encountered by W. Madelung and M. E. Oberwegner.¹⁰ Desyl chloride (IV) is converted into the oxides (V) and (VI) when treated with potassium hydroxide in toluene and with sodium methoxide respectively. On standing, (VI) is converted into the *cis*-form of the dioxan derivative (VII), from which the *trans*-form is obtained by treatment with methyl-alcoholic hydrogen chloride; the *trans*-form of (VII) is also produced directly from benzoin on treatment with methyl-alcoholic hydrogen chloride. Dehydration of (VII) leads to (VIII), from which four stereoisomeric tetrahydro-derivatives (IX) have been prepared. A dioxan structure (X) has been intro-



duced for the "chloro-diphenaclys" obtained by the action of sodium ethoxide on ω -chloroacetophenone,¹¹ but no satisfactory explanation has been advanced for the rearrangement of (X) during reduction to $\alpha\beta$ -dibenzoylthane.*

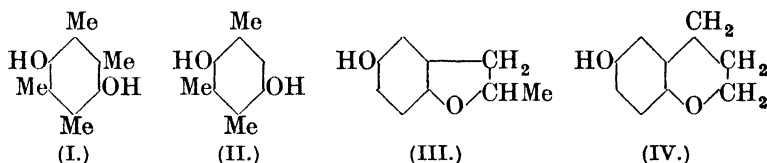
The Tocopherols.—The isolation, from the unsaponifiable fraction of wheat germ and cotton seed oils, of compounds possessing vitamin-E activity was discussed in these Reports for 1937 (p. 410).

¹⁰ W. Madelung and M. E. Oberwegner, *Annalen*, 1931, **490**, 201; 1936, **526**, 195.

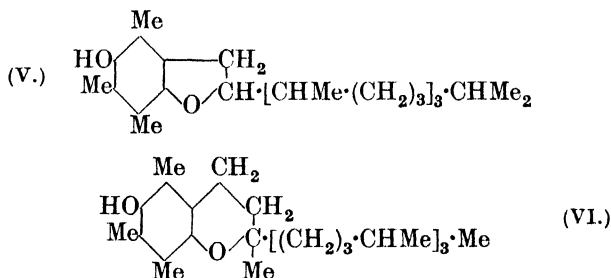
¹¹ O. Widman, *ibid.*, 1913, **400**, 90.

* Similar peculiar rearrangements have been reported for bimolecular lactolides (M. Bergmann, A. Miekeley, and E. von Lippmann, *Ber.*, 1929, **62**, 1467; M. Bergmann and A. Miekeley, *ibid.*, p. 2297).

The substances, previously known as neotocopherol¹² and cumotocopherol,¹³ have now been proved identical with β -tocopherol.^{14, 15, 16} The first indication of the constitution of the tocopherols was obtained by thermal decomposition at 350°; α - and β -tocopherol yielded duroquinol (I)¹⁷ and ψ -cumoquinol (II)¹³ respectively. Examination of a number of synthetic esters of the quinols (I) and (II) showed that they differed from the tocopherols in absorption



spectra and in their reactions with oxidising and hydrolytic agents.^{14, 16, 18} Consequently it was suggested that the C₂₀ side chain of the tocopherols was attached to the quinol nucleus by a carbon-carbon linkage, and a compound of structure (III) or (IV), synthesised from quinol and allyl bromide,¹⁴ resembled the



tocopherols in absorption spectrum. This synthetic reaction has been extended and modified, and racemic α -tocopherol, (V) or (VI), has been obtained from ψ -cumoquinol (II) by condensation with phytol bromide,¹⁹ phytol²⁰ or phytadiene.²¹ The synthetic

¹² P. Karrer, H. Salomon, and H. Fritzsche, *Helv. Chim. Acta*, 1937, **20**, 1422.

¹³ W. John, *Z. physiol. Chem.*, 1937, **250**, 11.

¹⁴ P. Karrer, H. Salomon, and H. Fritzsche, *Helv. Chim. Acta*, 1938, **21**, 309.

¹⁵ F. Bergel, A. R. Todd, and T. S. Work, *J.*, 1938, 253.

¹⁶ W. John, E. Dietzel, and P. Gunther, *Z. physiol. Chem.*, 1938, **252**, 201.

¹⁷ E. Fernholz, *J. Amer. Chem. Soc.*, 1937, **59**, 1154.

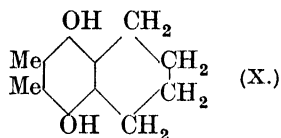
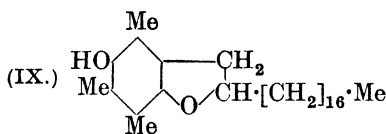
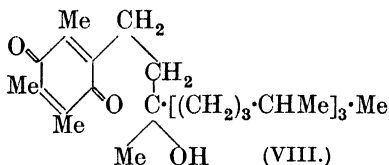
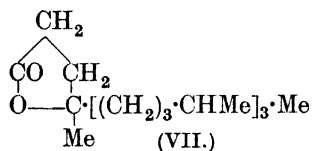
¹⁸ E. Fernholz, *ibid.*, 1938, **60**, 700.

¹⁹ P. Karrer, H. Fritzsche, B. H. Ringier, and H. Salomon, *Helv. Chim. Acta*, 1938, **21**, 520, 820.

²⁰ F. Bergel, (Miss) A. M. Copping, (Miss) A. Jacob, A. R. Todd, and T. S. Work, *J.*, 1938, 1382.

²¹ L. I. Smith, H. E. Ungnade, and W. W. Prichard, *Science*, 1938, **88**, 40.

racemate, which shows marked vitamin-E activity, has been resolved¹⁹ and the *d*-bromocamphorsulphonate is identical with that obtained from natural α -tocopherol. The synthesis outlined above is ambiguous and difficulties have been encountered in differentiating between the alternative structures (V) and (VI), but the latter chroman structure (VI) is now favoured by the specialists in this field. When α -tocopherol is oxidised with chromic acid or potassium permanganate,^{18, 22} the aromatic nucleus is destroyed and a γ -lactone, $C_{21}H_{44}O_2$, is obtained. The alcoholic group of the corresponding hydroxy-acid is inert and therefore probably tertiary in character, and the lactone is formulated as (VII). Further evidence in support of (VI) is obtained by oxidising α -tocopherol with silver nitrate or ferric chloride. A quinone is produced and this is regarded as (VIII) because the di-*p*-bromobenzoate of the corresponding quinol is not attacked by chromic acid.²³ The formation of the



quinone (VIII) may be followed by potentiometric titration with auric chloride, and the tertiary nature of the hydroxyl group of (VIII) is also indicated by its stability to aluminium *isobutoxide*.²⁴

Examination of a number of synthetic products shows that removal of methyl groups from the aromatic nucleus or modification of the side chain of α -tocopherol reduces the vitamin-E activity.²⁵ The coumaran (IX) is inactive,²⁶ but a variety of duroquinol ethers²⁷ and the compound (X)²⁸ show activity in large dosages.

β -Tocopherol has inferior vitamin-E activity, but its chemical

²² O. H. Emerson, *Science*, 1938, **88**, 40.

²³ W. John, E. Dietzel, P. Gunther, and W. Emte, *Naturwiss.*, 1938, **26**, 366.

²⁴ P. Karrer, R. Escher, H. Fritzsche, H. Keller, B. H. Ringier, and H. Salomon, *Helv. Chim. Acta*, 1938, **21**, 939.

²⁵ P. Karrer and K. A. Jensen, *ibid.*, p. 1622; W. John, P. Gunther, and M. Schmeil, *Ber.*, 1938, **71**, 2637.

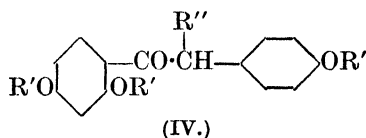
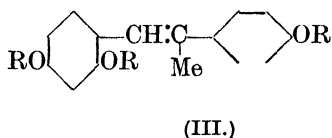
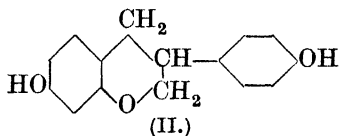
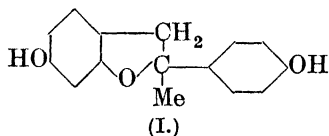
²⁶ F. Bergel, (Miss) A. Jacob, A. R. Todd, and T. S. Work, *J.*, 1938, 1375.

²⁷ F. Weider and T. Moll, *Z. physiol. Chem.*, 1938, **254**, 39.

²⁸ W. John and P. Gunther, *ibid.*, p. 51.

properties are similar to those of α -tocopherol. The compounds are not isomeric, and although the structure of β -tocopherol has not been established, the formation of ψ -cumoquinol instead of duroquinol on pyrolysis suggests that it is probably the lower homologue of α -tocopherol.

Equol.—Similar difficulty in distinguishing between chroman and coumaran structure has been encountered in an investigation on equol. This optically active dihydroxyphenol, $C_{15}H_{14}O_3$, isolated from horse urine,²⁹ yields a number of phenols and phenolic acids on fusion with alkalis. One of the products is an optically inactive, unsaturated, trihydroxyphenol, which as a result of recent work³⁰ is regarded as (III; R = H), and the structure is confirmed by a synthesis of the methyl ether (III; R = Me). Condensation of resorcinol with *p*-hydroxyphenylacetonitrile gave the trihydroxy-deoxybenzoin (IV; R' = R'' = H), the trimethyl ether (IV;



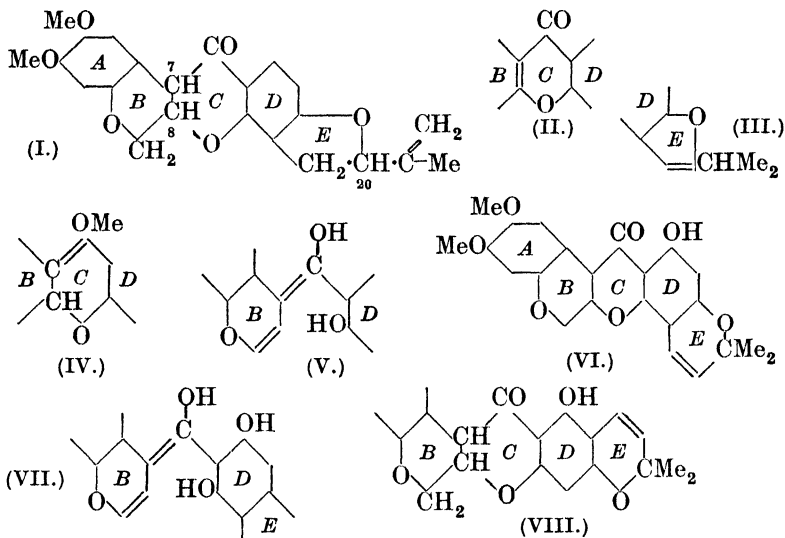
R' = Me, R'' = H) of which yielded (IV; R' = R'' = Me) on treatment with methyl iodide and sodium ethoxide. Pondorff reduction of (IV; R' = R'' = Me) and subsequent dehydration of the secondary alcohol yielded (III; R = Me). On the basis of this evidence structure (I) or (II) has been advanced for equol, but a decision between the alternatives has not been made.

Derris Constituents.—The structures of the constituents of derris root were reviewed in these Reports for 1937 (p. 346), and the reactions of *l*-rotenone were interpreted on the basis of structure (I), which contains three asymmetric carbon atoms at 7, 8, and 20. *l*-Dehydrorotenone (II), with asymmetry at position 20, and *l*-isorotenone (III), with asymmetry at positions 7 and 8, are obtained by the action of iodine and acetic-sulphuric acid respectively on rotenone (I). As both these derivatives (II) and (III) are lævoro-rotatory, it is legitimate to assign a lævoro-rotatory contribution to

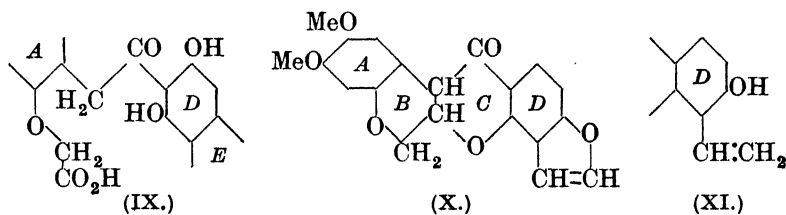
²⁹ G. F. Marrian and G. A. D. Haslewood, *Biochem. J.*, 1932, **26**, 1227; G. F. Marrian and D. Beall, *ibid.*, 1935, **29**, 1586.

³⁰ F. Wessely, H. Herschel, and G. Schlogl-Petzival, *Monatsh.*, 1938, **71**, 215.

C_{20} and also to the combination of C_7 and C_8 . When *l*-rotenone (I) is treated with alkali in benzene, methyl alcohol or acetone, but not in water, it is converted into mutarotenone, which is an equilibrium mixture of rotenone and *d*-epirotenone. As *d*-epirotenone may be



oxidised to *l*-dehydrototenone (II) and isomerised by acetic-sulphuric acid to *d*-isorotenone, it follows that *d*-epirotenone is derived from rotenone by inversion of both C_7 and C_8 . A similar inversion of both C_7 and C_8 must also be postulated in order to account for the formation of a *dl*-enol ether of type (IV) from *l*-isorotenone, and the inversions are explained by enolisation of C_7 and fission of ring *C* with the production of intermediate compounds of type (V).



This suggestion is supported by the observation that, in the presence of alkali, α -toxicarol (VI) is equilibrated with the isomeric β -toxicarol, and structure (VIII) assigned to the latter is consistent with the intermediate production of (VII) by enolisation and ring scission. On dehydrogenation, β -toxicarol is converted into dehydro- β -toxicarol (type II), which differs from dehydro- α -toxicarol. This

proves that α - and β -toxicarol contain different ring systems. Further reduction of the chromen ring of β -toxicarol yields a dihydro-derivative, which may be converted into a dehydrodihydro-derivative (type II), and the conversion of the last into the acid (IX), identical with the acid obtained similarly from α -toxicarol, completes the proof of the structure (VIII) for β -toxicarol.³¹

Further investigations on the constituents of derris have revealed the presence of *l*-toxicarol, which is converted into optically inactive α -toxicarol by the action of alkali,^{31, 32} and structures (X) and (XI), the former of which is more consistent with the analytical results, have been suggested³³ for a substance first isolated from derris by T. A. Buckley.³⁴

Rottlerin.—This yellowish-brown phenol, which was isolated in 1855 from the Indian colouring matter and anthelmintic drug known as kamala, has formed the subject of numerous researches, and the molecular formula of rottlerin has been a subject of controversy. H. Brockmann and K. Maier³⁵ have recently suggested the $C_{30}H_{28}O_8$ formula, which agrees with earlier analytical results.³⁶ Rottlerin contains two ethylenic linkages and five hydroxyl groups, which may be acylated or alkylated. Alkaline fission of rottlerin and tetrahydrorottlerin yields the dihydroxyphenol, rottlerone, and its tetrahydro-derivative respectively, together with *C*-methylphloroglucinol.³⁶ The conversion of tetrahydrorottlerone into β -phenylpropionic acid and 5 : 6-dihydroxy-2 : 2-dimethylchroman under the influence of hot concentrated alkali led to the suggestion of structure (I) or (II) for rottlerone.³⁷ The *C*-methylphloroglucinol derivative (III) has been obtained by the action of diazoaminobenzene on rottlerin and the structure has been established synthetically.³⁵ Analogy with the work of R. Boehm³⁸ indicated that the reaction with diazoaminobenzene was due to the presence of a methylenebisphloroglucinol group and it was inferred that the *C*-methylphloroglucinol and rottlerone residues are united as in (IV) or (V). Rottlerin is isomerised by boiling with alcohol to *isorottlerin*,³⁵ which contains a single ethylenic bond and does not

³¹ R. S. Cahn, R. F. Phipers, and J. J. Boam, *J.*, 1938, 513, 734.

³² F. Tattersfield and J. J. Martin, *J. Soc. Chem. Ind.*, 1937, 56, 77r.

³³ S. H. Harper, *Chem. and Ind.*, 1938, 57, 1509; R. S. Cahn and J. J. Boam, *J.*, 1938, 1818.

³⁴ *J. Soc. Chem. Ind.*, 1936, 55, 285r.

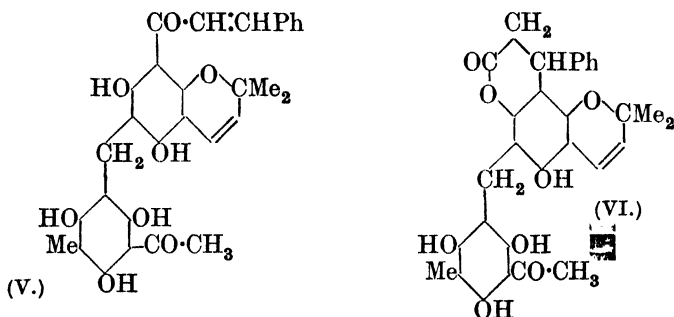
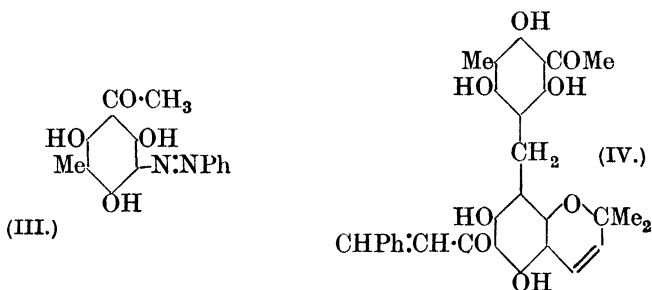
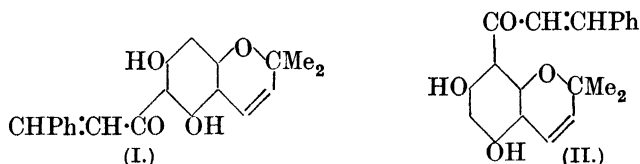
³⁵ *Annalen*, 1938, 535, 175.

³⁶ A. McGookin, F. P. Reed, and A. Robertson, *J.*, 1937, 748. K. S. Narang and B. S. Ray (*Current Sci.*, 1936, 6, 608) prefer the $C_{31}H_{30}O_8$ formula proposed by A. Hoffman and L. Faier (*Arch. Pharm.*, 1933, 271, 97).

³⁷ A. McGookin, A. B. Percival, and A. Robertson, *J.*, 1938, 309.

³⁸ *Annalen*, 1901, 318, 262.

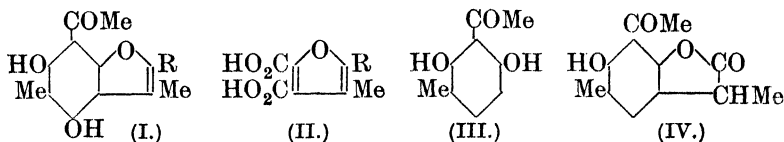
react with diazoaminobenzene. On the basis of structure (V) for rottlerin, formula (VI) was suggested for *isorottlerin*. A final decision between structures (IV) and (V) for rottlerin has not been made. Structure (IV) can accommodate two isomeric *isorottlerins*; the isolation of one form only does not exclude structure (IV), as steric factors may inhibit the formation of the other isomer.



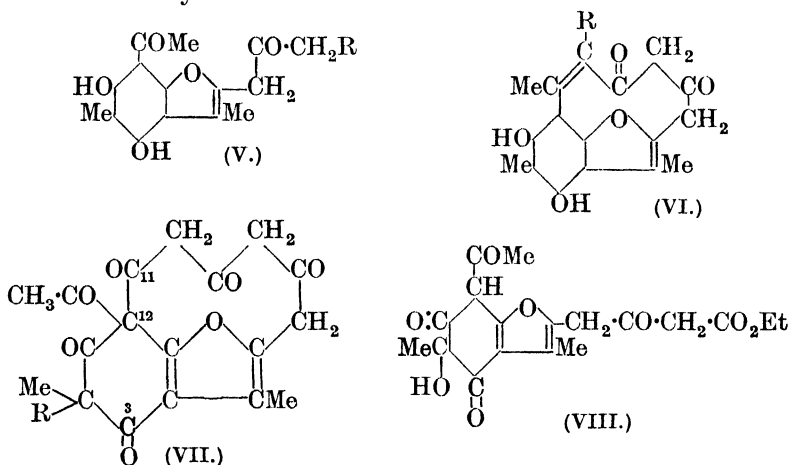
4-Arylresorcinols of known constitution are readily soluble in alkali and the sparing solubility of rottlerone has been used as an argument in favour of (I) and (IV) for rottlerone and rottlerin respectively.³⁷

Usnic Acid.—Considerable progress has been made since the chemistry of usnic acid, which occurs in many lichens, was last reviewed (*Ann. Reports*, 1933, **30**, 224). It is now generally agreed that the acidic properties of usnic acid, $C_{18}H_{16}O_7$, are due to a reactive β -diketonic group. The presence of a coumaran nucleus is indicated by the frequent isolation of coumaran derivatives from degradation experiments. Thus alkali converts usnic acid into acetoacetic acid

and usnetic acid (I; $R = CH_2 \cdot CO_2H$), which is decarboxylated to usnetol (I; $R = Me$), and the structure of the latter has been proved



by synthesis.³⁹ The orientation of the furan ring of (I; $R = CH_2 \cdot CO_2H$) is proved by oxidation with hydrogen peroxide to the tribasic acid (II; $R = CH_2 \cdot CO_2H$).⁴⁰ The isonitroso-derivative of (II; $R = CH_2 \cdot CO_2H$) was converted into the nitrile (II; $R = CN$), which yielded the known 3-methylfuran-2-carboxylic acid on decarboxylation and subsequent hydrolysis. As usnetic acid differs from the synthetic isomer derived by interchanging the Me and $CH_2 \cdot CO_2H$ groups in (I; $R = CH_2 \cdot CO_2H$),⁴¹ its structure is rigidly established. More recently, compounds (III) and (IV) have been obtained by degradation of dihydrousnic acid⁴² and the suggested structures have received synthetical confirmation.⁴³



When usnic acid is heated with absolute and 96% alcohol at 150° , it is converted into acetousnetic ester (V; $R = CO_2Et$)⁴⁴ and decarbousnic acid (V; $R = CO \cdot CH_3$) respectively.^{45, 46} The latter

³⁹ F. H. Curd and A. Robertson, *J.*, 1933, 1174.

⁴⁰ Y. Asahina and M. Yanganita, *Ber.*, 1937, **70**, 1500.

⁴¹ H. F. Birch, D. G. Flynn, and A. Robertson, *J.*, 1936, 1834.

⁴² Y. Asahina and M. Yanganita, *Ber.*, 1938, **71**, 2260.

⁴³ M. Yanganita, *ibid.*, p. 2269.

⁴⁴ Y. Asahina, M. Yanganita, and S. Mayeda, *ibid.*, 1937, **70**, 2462.

⁴⁵ O. Widman, *Annalen*, 1900, **310**, 230; 1902, **324**, 139

⁴⁶ F. H. Curd and A. Robertson, *J.*, 1937, 894.

β -diketone (V; $R = CO \cdot CH_3$) is dehydrated by sulphuric acid to decarbousnol, which is regarded as (VI; $R = H$).⁴³ There can be no steric objection to this novel structure (VI; $R = H$), which corresponds spatially to a phenanthrene system. Interaction between the carbonyl group and the furan oxygen atom, similar to that between the carbonyl and the methylimino-group in the alkaloid cryptopine, may be responsible for the inhibition in decarbousnol of certain β -diketonic properties. Usnolic acid, obtained from usnic acid by isomerisation with sulphuric acid, is a carboxylic acid, which yields decarbousnol (VI; $R = H$) on decarboxylation, and structure (VI; $R = CO_2H$) is consistent with the properties of usnolic acid.

The optical inactivity of the compounds discussed above is in agreement with the suggested formulæ. Usnic acid has, however, been obtained in *d*-, *l*-, and *dl*-modifications, and many of the properties, including the optical activity of the acid, are interpreted satisfactorily on the basis of the recently introduced⁴² structure (VII; $R = H$). Hydrolysis at the 11 : 12-bond and subsequent aromatisation to the *C*-methylphloroglucinol type accounts for the optically inactive degradation products; the side chain liberated during the hydrolysis may either recombine with the nuclear $CO \cdot CH_3$ group, as in the formation of (VI), or suffer degradation to structure (IV) or (I). Dihydrousnic acid is assumed to be the secondary alcohol produced by reduction of the exposed carbonyl group in position 3, and formation of (III) and (IV) is preceded by dehydration of this secondary alcoholic group.

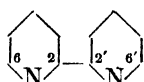
Structure (VII; $R = H$) for usnic acid also gives a satisfactory explanation of the properties of usnonic acid, $C_{18}H_{16}O_8$, which is prepared by the action of potassium permanganate or lead tetra-acetate on usnic acid.^{42, 44, 45} Usnonic acid is optically active and as it is reduced by zinc and acetic acid to optically active usnic acid, it is regarded as (VII; $R = OH$). When heated with alcohol at 150° , usnonic acid is converted into optically active *isooxy*-acetousnetic ester (VIII), but it is reduced by zinc and acetic acid to inactive acetousnetic ester (V; $R = CO_2Et$). Such behaviour is consistent with structure (VII; $R = OH$) for usnonic acid; the chinol-benzene rearrangement responsible for the loss of optical activity is prevented by the hydroxyl group of (VIII), but replacement of the group by hydrogen leads to rapid rearrangement to the inactive aromatic form.

(b) Nitrogen Ring Compounds.

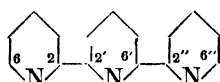
Pyridine and Polypyridyls.—When pyridine is brominated in the vapour phase at high temperatures and in the presence of a catalyst,

an abnormal reaction leading to substitution in the α -positions predominates. Thus at 300° in the presence of carbon or pumice, 3-bromo- and 3:5-dibromo-pyridines are obtained in 39% and 15% yields respectively, but at 500° , 48% and 36% yields of 2-bromo- and 2:6-dibromo-pyridines respectively are produced. With a ferrous or cuprous bromide catalyst, however, abnormal attack of the 2- and 6-positions occurs at 300° .¹ Equally remarkable results have been obtained in the benzene series and chloro- and bromo-benzene are substituted in the *m*-positions above 450° .²

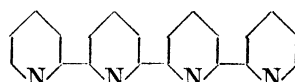
This work has been extended at the Teddington laboratories and an interesting series of polypyridyls, giving a multitude of metallic



(I.)



(II.)



(III.)

co-ordination compounds, has been obtained.³ 2:2'-Dipyridyl (I) has been prepared in 70% yields by dehalogenation of 2-bromopyridine with copper in boiling diphenyl solution, and under similar conditions a mixture of 2-bromo- and 2:6-dibromopyridine is converted into 2:2':2''-tripyridyl (II) and 2:2':2'':2'''-tetrapyridyl (III). This reaction proves the constitution of bases (II) and (III), which, however, may be more conveniently prepared by dehydrogenating pyridine with ferric chloride,⁴ and 2:2'-dipyridyl with iodine respectively. When 2:2'-dipyridyl is brominated at 500° , 6-bromo- and 6:6'-dibromo-derivatives are obtained, and the structures of the substitution products are established by the conversion of the former, or a mixture of the latter with 2-bromopyridine, into 2:2':2'':2'''-tetrapyridyl (III) by dehalogenation with copper. Similar high-temperature bromination of (II) gave 6-bromo- and 6:6''-dibromo-tripyridyl, and dehalogenation of the former yielded 2:2':2'':2''' : 2'''' : 2'''''-hexapyridyl, which, however, is best prepared by the action of iodine on 2:2':2'':2'''-tripyridyl (II). Dehalogenation of a mixture of 6:6''-dibromo-2:2':2''-tripyridyl and 2-bromopyridine yielded 2:2':2'':2''' : 2''''-pentapyridyl.

Glucazidone.—The formation of quinoxaline derivatives from *o*-phenylenediamine and α -keto-acids has been investigated.⁵

¹ H. J. den Hertog and J. P. Wibaut, *Rec. Trav. chim.*, 1933, **51**, 381, 940.

² J. P. Wibaut, L. M. F. Lande, and G. Wallagh, *ibid.*, 1933, **52**, 794; 1937, **56**, 65; J. P. Wibaut and M. von Loon, *ibid.*, 1937, **56**, 815.

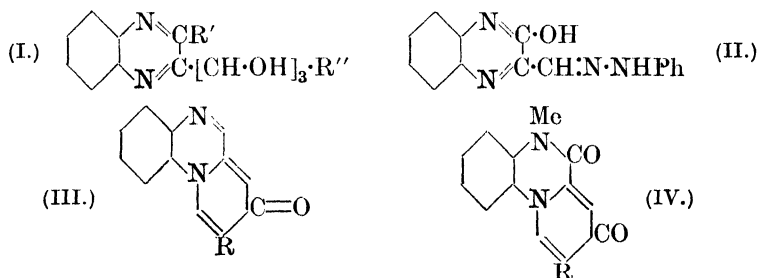
³ F. H. Burstall, *J.*, 1938, 1662; (Sir) G. T. Morgan and F. H. Burstall, *ibid.* pp. 1672, 1675.

⁴ G. T. Morgan and F. H. Burstall, *J.*, 1932, 20; 1934, 1498.

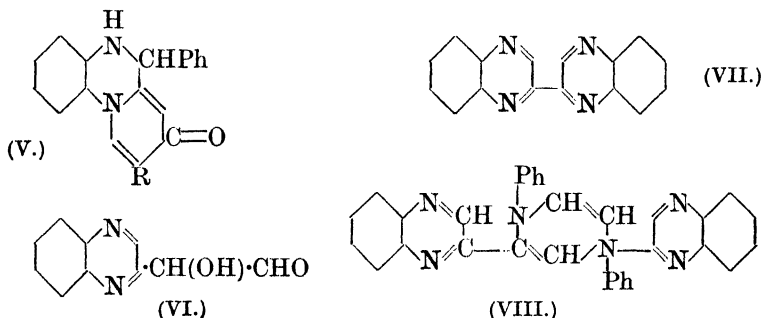
⁵ H. Ohle, *Ber.*, 1934, **67**, 155; H. Erlbach and H. Ohle, *ibid.*, p. 555; H. Ohle and W. Gross, *ibid.*, 1935, **68**, 2262.

Condensation with α -ketogluconic acid yielded the quinoxaline (I; $R' = OH$, $R'' = CO_2H$), the structure of which was indicated by oxidation to 2:3-dihydroxyquinoxaline, and by conversion into the hydrazone (II) by the action of phenylhydrazine. The hydrazone (II) was also obtained from the condensation product of *o*-phenylenediamine and dibromopyruvic acid.

In 1887, P. Griess prepared similar quinoxalines from glucose and *o*-phenylenediamine. The compounds have been reinvestigated and it has been shown that fructose, glucose, and sucrose yield the quinoxaline (I; $R' = H$, $R'' = CH_2 \cdot OH$), but galactose and the pentoses give benziminazole derivatives.⁶ The quinoxaline



derivative (I; $R' = H$, $R'' = CH_2 \cdot OH$) is degraded to quinoxaline under the influence of light,⁷ and it is converted into glucazidone (III; $R = H$), together with a little hydroxyglucazidone (III; $R = OH$) by the action of sulphuric acid.⁶ Glucazidone (III; $R =$



H), unlike (I; $R' = H$, $R'' = CH_2 \cdot OH$), is optically inactive and non-reducing, and it is oxidised by potassium permanganate to quinoxaline-2-carboxylic acid. With methyl iodide, glucazidone (III; $R = H$) gives a quaternary salt, which is oxidised by ferricyanide to the compound (IV; $R = H$), and the action of phenyl-

⁶ K. Maurer and B. Schiedt, *Ber.*, 1934, **67**, 1800; K. Maurer, B. Schiedt, and H. Schroeter, *ibid.*, 1935, **68**, 1716.

⁷ R. Kuhn and F. Bar, *ibid.*, 1934, **67**, 898.

magnesium bromide on glucazidone leads to a secondary amine which is regarded as (V; R = H) because it is oxidised to 3-phenyl-quinoxaline-2-carboxylic acid. The structure (III; R = OH) assigned to hydroxyglucazidone is supported by the conversion of the *O*-methyl ether into (IV; R = OMe) and (V; R = OMe). When the quinoxaline (I; R' = OH, R'' = CH₂·OH) is treated with sodium methoxide, a red product containing (VI) is obtained. This substance, which gives an acetyl derivative and a semicarbazone, yields quinoxaline-2-carboxylic acid on oxidation, reacts with *o*-phenylenediamine to give the diquinoxaline (VII), and the anil of (VI) polymerises to a compound for which structure (VIII) is suggested.⁸

Glyoxaline Derivatives.—The early Radziszewski synthesis of glyoxalines from glyoxal, formaldehyde, and ammonia has been modified with great improvement in yield and application. When a mixture of an α -hydroxy-aldehyde or -ketone is allowed to react in the cold with ammonia and an aldehyde in the presence of copper acetate, the glyoxaline derivative is precipitated in excellent yield as a complex copper salt.⁹ The hydroxy-ketone and aldehyde components may be aromatic or aliphatic, and *cyclohexanone* has been used in the preparation of tetrahydrobenzoglyoxalines.¹⁰ When fructose is employed as the hydroxy-ketonic component, 4-hydroxymethylglyoxaline is obtained, presumably by scission of the fructose into trioses, and the observation is of considerable interest in connection with the biological formation of histidine derivatives.¹¹

Cupric ions also have a marked influence on the yields of benziminazoles obtained by the Ladenburg-Hinsberg synthesis from *o*-phenylenediamines and aldehydes and extensive applications of the method are described.¹²

Phenazine Derivatives.—The physiological activity of phenazine derivatives and the frequent occurrence of the phenazine nucleus in the structure of the bacterial pigments has led to much activity in this field.

Oxychlororaphine, the yellow pigment of *Bacillus chlororaphis*, has been shown to be the amide (I; R = CO·NH₂) of phenazine-1-carboxylic acid (I; R = CO₂H). The phenazine nature of the pigment was first proved by hydrolysis and decarboxylation to phenazine, and the position of the amido-group was established by

⁸ K. Maurer and B. Boettger, *Ber.*, 1938, **71**, 1383, 2092.

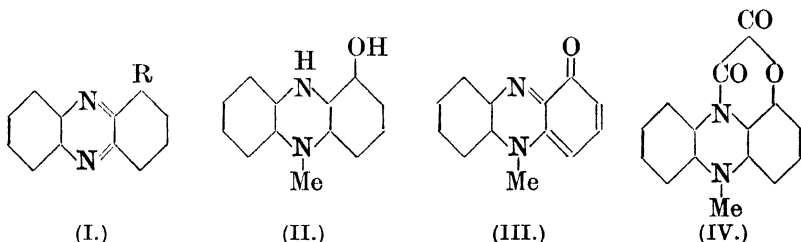
⁹ R. Weidenhagen and R. Herrmann, *ibid.*, 1935, **68**, 1953, 2205.

¹⁰ R. Weidenhagen and H. Wegner, *ibid.*, 1938, **71**, 2124.

¹¹ *Idem*, *ibid.*, 1937, **70**, 570.

¹² R. Weidenhagen, *ibid.*, 1936, **59**, 2263; R. Weidenhagen and V. Weeded *ibid.*, 1938, **71**, 2347.

synthesis, Wohl's method being used. Nitrobenzene and anthranilic acid were heated with potassium hydroxide; a small yield of (I; $R = CO_2H$) was obtained and the corresponding amide (I; $R = CO \cdot NH_2$) was identical with oxychlororaphine.¹³ A second synthesis has been effected under milder conditions; 1-methyl-1:2:3:4-tetrahydrophenazine, obtained from *o*-phenylenediamine and 1-methylcyclohexan-2:3-dione, was dehydrogenated to 1-methylphenazine, which on oxidation gave (I; $R = CO_2H$).¹⁴



F. Wrede and E. Strack¹⁵ showed that pyocyanine, the blue pigment of *B. pyocyaneus*, underwent oxidative *N*-demethylation to 1-hydroxyphenazine (I; $R = OH$) when its alkaline solutions were exposed to air. Structure (I; $R = OH$) was established by synthesis from 3-methoxy-*o*-benzoquinone and *o*-phenylenediamine, and subsequent demethylation with hydrobromic acid. Reduction with zinc and acetic acid converted pyocyanine into a dihydro-derivative, which was regarded as (II) and gave pyocyanine on autoxidation. Pyocyanine was therefore formulated as (III) and it was synthesised by the action of alkalis on 1-hydroxyphenazine methosulphate. Pyocyanine has also been synthesised in 45% yields by exposing aqueous solutions of phenazine methosulphate to sunlight for one day.¹⁶ The above experiments, however, do not establish the relative positions of the OH and NH groups in dihydrophenazine (II), but it has been shown that oxalyl chloride converts dihydrophenazine into a cyclic compound (IV),¹⁷ thus proving structure (II) for dihydrophenazine and supporting (III) for pyocyanine. The physical properties of the pigment are, however, more in agreement with the dipole modification (V).

The crystalline purple pigment, $C_{12}H_8O_4N_2$, of *Chromobacterium iodinum* has been proved to be a phenazine derivative.¹⁸ Catalytic

¹³ F. Kogl and J. J. Postowsky, *Annalen*, 1930, **480**, 280; F. Kogl and B. Tonnies, *ibid.*, 1932, **497**, 265.

¹⁴ G. R. Clemo and H. McIlwain, *J.*, 1934, 1991.

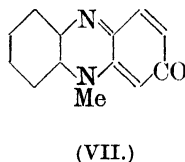
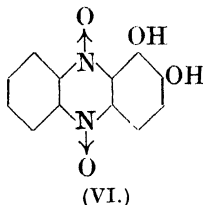
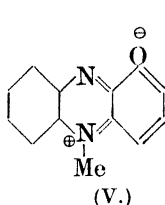
¹⁵ *Z. physiol. Chem.*, 1925, **142**, 803; 1928, **177**, 177; 1929, **181**, 58; *Ber.*, 1929, **62**, 2051.

¹⁶ H. McIlwain, *J.*, 1937, 1708.

¹⁷ H. Hillemann, *Ber.*, 1938, **71**, 46.

¹⁸ G. R. Clemo and H. McIlwain, *J.*, 1938, 479.

reduction yielded a colourless substance, $C_{12}H_{10}O_2N_2$, which underwent autoxidation to a dihydroxyphenol, $C_{12}H_8O_2N_2$; this gave phenazine on distillation with zinc. The pigment liberates iodine from iodides, the absorption spectrum resembles those of the di-*N*-oxides prepared by the action of hydrogen peroxide on phenazine



or 1-hydroxyphenazine, and structure (VI) has been advanced for the pigment. The position of the hydroxyl groups is indicated by the formation of metallic lakes from the dihydroxyphenol, $C_{12}H_8O_2N_2$.

It will be convenient to refer at this point to a number of observations made in a more general study of phenazine derivatives. 1 : 2 : 3 : 4-Tetrahydrophenazine and its derivatives, obtained from appropriate *o*-phenylenediamines and *cyclohexane*-1 : 2-diones, have been reduced either to 1 : 2 : 3 : 4 : 9 : 10-hexahydrophenazine, which has been isolated in *cis*- and *trans*-forms, or to 1 : 2 : 3 : 4 : 5 : 6 : 7 : 8-octahydrophenazine.¹⁹ 1 : 2 : 3 : 4-Tetrahydrophenazine and benzaldehyde condense to give 1 : 4-dibenzylphenazine :²⁰ the isomeric dibenzylidene structure is excluded by the stability of the product towards oxidising agents. The reactivity of the 1- and 4-methylene groups in tetrahydrophenazine has numerous analogies in heterocyclic chemistry and the activity of tetrahydroacridine and 7-aza-5 : 6-benzohydrindene²¹ may be cited as recent examples. Examination of the *N*-alkylphenazonium salts has shown that facile substitution occurs in the 2-, 4-, and 10-positions and that oxidative *N*-demethylation, similar to that mentioned above in the case of pyocyanine, is frequently observed. In absence of air *N*-methylphenazonium hydroxide solutions decompose into formaldehyde, phenazine and *N*-methyl-9 : 10-dihydrophenazine,²² but in presence of oxygen the last is partially oxidised and 5% yields of 2-keto-*N*-methylphenazine (VII) are produced. The conversion of phenazine methosulphate into pyocyanine, mentioned above, is accompanied by phenazine and the decomposition provides a further example of *N*-demethylation and substitution in position 4. When treated with potassium cyanide and with sodium sulphite,

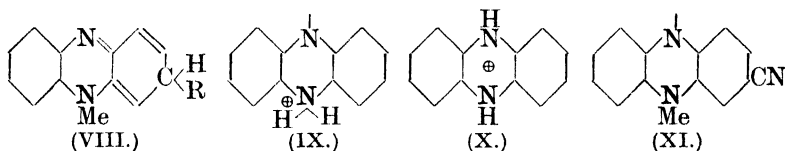
¹⁹ G. R. Clemo and H. McIlwain, *J.*, 1936, 258, 1698.

²⁰ H. McIlwain, *J.*, 1937, 1701.

²¹ W. Borsche and R. Manteuffel, *Annalen*, 1938, 534, 56.

²² H. McIlwain, *J.*, 1937, 1704.

phenazine methosulphate is converted into compounds regarded as (VIII; $R = CN$) and (VIII; $R = SO_3Na$) respectively. These structures, which postulate substitution in the 2-position, are based on analogy, but structure (VIII; $R = CN$) is consistent with the conversion of the nitrile, by heat and subsequent hydrolysis, into



phenazine-2-carboxylic acid. Nuclear methylation, assumed to be in position 2, is observed during the prolonged action of methyl sulphate on phenazine, and substitution in position 10 is encountered in the formation of 9 : 10-dimethyl-9 : 10-dihydrophenazine together with phenazine when phenazine methiodide is treated with methylmagnesium iodide.²³

The reduction of the pale yellow phenazines to the colourless 9 : 10-dihydro-compounds and the reverse dehydrogenation proceed through intermediate green salts. These salts were investigated by A. Hantzsch, who showed their resemblance to the quinhydrones, but suggested a unimolecular radical structure. Potentiometric measurements show clearly that the reduction of a phenazine salt occurs in two stages, and the intermediate green salt may be formulated as the radical (IX) or its equivalent (X).²⁴ Reduction of phenazine methosulphate with one atom of hydrogen gives a green sulphate, the cation of which is the radical (X; with NMe instead of NH). Addition of a second hydrogen atom yields colourless 9-methyl-9 : 10-dihydrophenazine, and the reverse changes may be followed iodometrically.²³ Bases corresponding to the semiquinonoid salt (X) have been isolated. The nitrile (VIII; $R = CN$), obtained from potassium cyanide and phenazine methosulphate, is autoxidised to a blue crystalline radical (XI), and the *N*-ethylphenazyl radical (XI; with H and Et instead of CN and Me respectively) was obtained by the action of air on 9-ethyl-9 : 10-dihydrophenazine. In these cases the unimolecular structure was supported by cryoscopic measurements.²² In the same way the red salts of pyocyanine are reduced to intermediate green salts possessing a radical cation, and similar coloured radicals have been encountered during reduction of lactoflavin,²⁵ pyridine alkyl halides,²⁶ and aneurin.²⁷

²³ H. Hillemann, *Ber.*, 1938, **71**, 34.

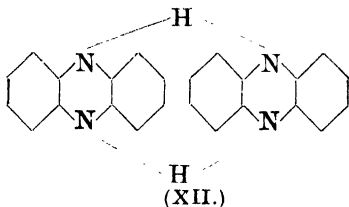
²⁴ L. Michaelis, *Chem. Reviews*, 1935, **16**, 243.

²⁵ R. Kuhn and R. Ströbele, *Ber.*, 1937, **70**, 753.

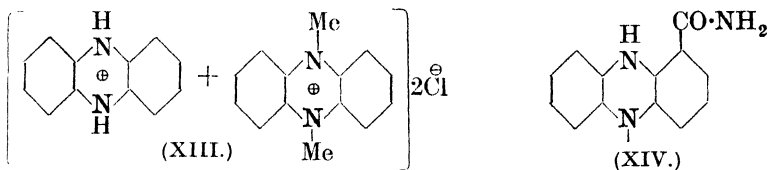
²⁶ P. Karrer and F. Benz, *Helv. Chim. Acta*, 1936, **19**, 1028; P. Karrer and F. J. Stare, *ibid.*, 1937, **20**, 418.

²⁷ F. Lipmann and G. Perlman, *J. Amer. Chem. Soc.*, 1938, **60**, 2574.

Crystalline blue compounds known as phenazhydrins²⁸ are obtained by mixing equimolecular proportions of phenazine and dihydrophenazines. The phenazhydrins differ from the phenazyl radicals and resemble the quinhydrones, in dissociating to pale yellow solutions. Molecular-weight determinations cannot be made, but a resonance structure (XII) is required to explain the observation



that the phenazhydrin obtained from phenazine and 1-methyl-9:10-dihydrophenazine is identical with that obtained from 1-methylphenazine and 9:10-dihydrophenazine. The



phenazhydrin salts, which yield green solutions, are, however, assigned the radical structure (X), and in agreement with these views it was found that phenazine and 9:10-dimethyl-9:10-dihydrophenazine, although incapable of forming a phenazhydrin, yielded a complex green hydrochloride (XIII). The resonance structure for the phenazhydrins receives indirect support from the recent observation²⁹ that quinhydrone is diamagnetic; this excludes the radical formula but supports the resonance structure for quinhydrone.

The structure of oxychlororaphine has been discussed. Reduction with zinc and water produces a green pigment, known as chlororaphine, which is occasionally found in cultures of *B. chlororaphis*. This pigment was first regarded as a bimolecular complex of oxychlororaphine with its dihydro-derivative,¹³ but later the radical structure (XIV) was introduced.¹³ Potentiometric studies in acid solution³⁰ support the radical structure of the chlororaphine cation, but the constitution of the base must be regarded as uncertain. Chlororaphine dissociates in neutral solvents; this does not necessarily exclude the radical formula, but the general resemblance with the quinhydrones and phenazhydrins favours the bimolecular resonance formula for the pigment.

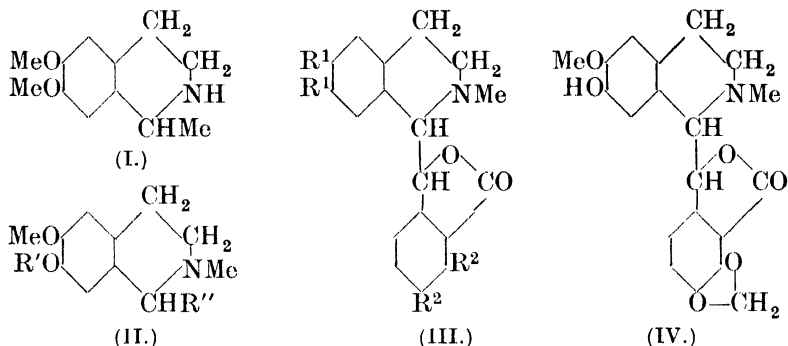
Alkaloids.—(a) *isoQuinoline alkaloids.* Base (I), synthesised by

²⁸ G. R. Clemo, and H. McIlwain, *J.*, 1934, 1991; 1935, 738.

²⁹ L. Michaelis, M. P. Schilbert, R. K. Riber, J. A. Kuck, and S. Granick, *J. Amer. Chem. Soc.*, 1938, 60, 1678.

³⁰ B. Elema, *Rec. Trav. chim.*, 1933, 52, 569.

standard methods, has been resolved and the *l*-form is identical with natural salsolidine.³¹ Structure (II; $R' = R'' = H$), assigned to corypalline, an alkaloid obtained from *Corydalis pallida* or the seeds of *C. aurea*,³²ⁿ has been confirmed by syntheses of the ethyl and the benzyl ether, and acid hydrolysis of the latter yielded a phenol identical with corypalline.



The investigation of corypalline forms part of a detailed examination made during the last six years on the alkaloidal constituents of American species of *Dicentra*, *Corydalis*, and *Adlumina*.³² Bases of the protopine, berberine, aporphine and narcotine types have been isolated, and the use of improved experimental methods has led not only to the isolation of many known bases but also to the discovery of some thirty new alkaloids. Protopine is a universal constituent of these American fumariaceous plants, but its association with cryptopine and α -*allo*-cryptopine in twelve species has not been observed previously in Asiatic varieties; this may be due partly to the use of superior methods and not necessarily to alkaloidal variations within the species. Corydaline and phenolic bases, including corypalline, *isocorypalline*, and *scoulerine*, have been isolated from both American and Asiatic varieties. Tetrahydropalmatine, which occurs as the *d*-form in the Asiatic plants, is present in *l*- and *dl*-forms in *C. aurea* ^{32h} and *C. caseana* ^{32g, 33} and a dihydroxyphenol, known as *aurotensine*, which gives 1-tetrahydropalmatine on methylation, is obtained from *C. aurea*.^{32p} The aporphine bases include *dicentrine*, *glaucine*, *corytuberine*, *corydine*,

³¹ E. Spath and F. Dongel, *Ber.*, 1938, **71**, 113.

³² R. H. F. Manske, *Canadian J. Res.*, (a) 1932, **7**, 258; (b) *ibid.*, p. 264; (c) 1933, **8**, 142; (d) *ibid.*, p. 210; (e) *ibid.*, p. 404; (f) *ibid.*, p. 407; (g) *ibid.*, p. 592; (h) 1933, **9**, 436; (i) 1934, **10**, 521; (j) *ibid.*, p. 765; (k) 1936, **14**, 325; (l) *ibid.*, p. 347; (m) *ibid.*, p. 354; (n) 1937, **15**, 159; (o) *ibid.*, p. 274; (p) *ibid.*, 1938, **16**, 81; (q) *ibid.*, p. 153.

³³ Private communication from Dr. Manske.

and bulbocapnine, and a new phenolic base, glaucentrine, obtained from three species of American *Dicentra*,^{32g, 4, f} is proved by methylation to be an *O*-demethylglauceine.

Bases of the narcotine group have not been previously isolated from the *Fumariaceæ*, but the structures of a number of newly discovered bases of this type have been established by standard oxidative hydrolysis to phthalaldehydic acids and 1-hydroxy-2-methyltetrahydroisoquinolines. The structure (III; $R^1R^1 = R^2R^2 = CH_2O_2$), derived for the alkaloid bicuculline^{32a, b} which has been isolated from nine American species, has been confirmed synthetically,³⁴ and bicucine^{32h} represents the corresponding hydroxy-acid. Adlumine, isolated as *d*- and *l*-forms from *Adlumina fungosa*^{32d} and *C. semperivens*^{32f} or *C. scouleri*³²ⁱ respectively, and corlumine, obtained from *C. siberica* and *C. scouleri*,^{32l, m} are diastereoisomeric forms^{32e, k} of (III; $R^1 = OMe$, $R^2R^2 = CH_2O_2$). Corlumidine,^{32k, l, n} a phenol present in *C. scouleri*, yields corlumine on methylation, and as ethylation and subsequent hydrolysis give the carbinol base (II; $R' = Et$, $R'' = OH$), which was also prepared by an unambiguous synthesis, structure (IV) is established for corlumidine. Cordrastine,^{32p} obtained from *C. aurea*, probably represents the tetramethoxy-analogue (III; $R^1 = R^2 = OMe$).

The constitutions of other bases isolated from the fumariaceous plants are uncertain, but relationships are frequently apparent. For instance, capaurine and capauridine,^{32h} from *C. aurea*, are isomeric bases, $C_{21}H_{27}O_5N$, containing one hydroxy- and four methoxy-groups; these must be differently oriented, as the alkaloids yield isomers on methylation. Adlumidine,^{32d} from *Adlumina fungosa*, and capnoidine,^{32f, i} from *C. scouleri* and *C. semperivens*, are isomeric methoxyl-free compounds, $C_{19}H_{15}O_6N$, probably belonging to the narcotine class. The phenolic dimethoxy-base, cularidine,^{32p} from *D. cucullaria*, its methyl ether, cularine,^{32p} obtained from *D. cucullaria*, *eximia*, *formosa*, and *oregana*, and *N*-demethylcularine,^{32p} from *D. eximia*, form a related group of bases containing an oxygen atom of unknown function.

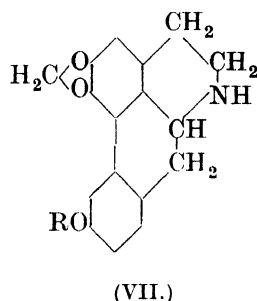
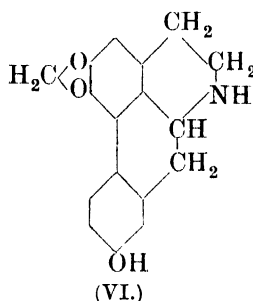
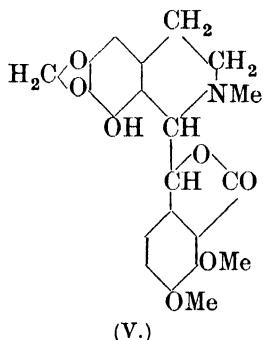
Structure (V) is consistent with the properties of narcotoline, a new phenolic base isolated from *Papaver somniferum*,³⁵ which yields narcotine on methylation and meconine on heating with acetic anhydride. Anolobine, $C_{17}H_{17}O_3N$, a phenolic secondary amine containing a methylenedioxy-group, has been isolated from the bark of *Asimina triloba*.³⁶ Methylation and alkali treatment

³⁴ P. W. G. Groenewoud and R. Robinson, *J.*, 1936, 199.

³⁵ F. Wrede, *Arch. Exp. Path. Pharm.*, 1937, **184**, 331.

³⁶ R. H. F. Manske, *Canadian J. Res.*, 1938, **16**, 76.

yield an optically inactive methin, $C_{20}H_{23}O_3N$, which gives 4-methoxyphthalic acid on exhaustive methylation and subsequent oxidation. Of the two structures (VI) and (VII; $R = H$) capable of accounting for these results, the latter is excluded because the methin $C_{20}H_{23}O_3N$ differs from that obtained from laureline (VII; $R = Me$).³⁷



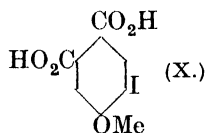
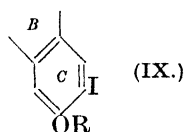
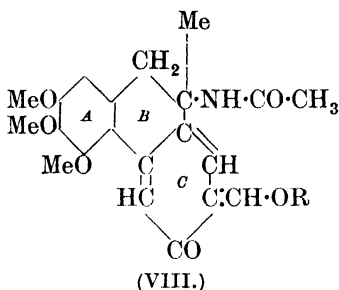
The structure of colchicine, the alkaloid of the autumn crocus, is still uncertain. Structures (VIII; $R = Me$) and (VIII; $R = H$) were suggested for colchicine and its hydrolysis product, colchicine, respectively as a result of the investigations of A. Windaus in 1923. The position of the three methoxyl groups was supported by oxidation to trimethoxyphthalic acid, and degradation to 9-methylphenanthrene and certain nitrogenous naphthalene derivatives proved that the methyl and the acetamido-group were attached to the 9- or the 10-position. The orientation of ring *C* was unsettled, but this is now limited to two possibilities. A. Windaus showed that, when treated with iodine, colchicine was converted into an iodophenol regarded as (IX; $R = H$), the methyl ether (IX; $R = Me$) of which gave an iodomethoxyphthalic acid on oxidation. R. Grewe³⁸ has synthesised the acid (X), which is identical with the colchicine degradation product, and it follows that the iodophenol must have either structure (IX; $R = H$) suggested by A. Windaus, or an alternative derived by interchanging the iodine atom and the hydroxyl group. Structure (VIII; $R = H$) represents colchicine as the hydroxymethylene form of a phenolic aldehyde and on general grounds the aromatic form would be regarded as stable. However, the absorption spectrum of colchicine (VIII; $R = H$) resembles that of colchicine (VIII; $R = Me$)³⁹ and it is concluded that colchicine exists in the hydroxymethylene form.

³⁷ G. Barger and A. Girardet, *Helv. Chim. Acta*, 1931, **14**, 481; E. Schittler, *ibid.*, 1932, **15**, 394.

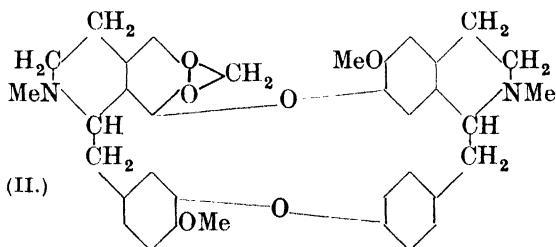
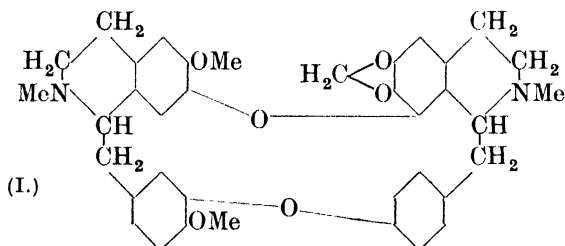
³⁸ *Ber.*, 1938, **71**, 245.

³⁹ K. Bursian, *ibid.*, p. 745.

The appearance of two new bands in the spectrum of the base in ammoniacal solution indicates partial transformation to the aromatic state, but the stability of the hydroxymethylene form and the failure to obtain an adduct with maleic anhydride are not consistent with the arrangement of double bonds in structure (VIII).⁴⁰



The structure of cepharanthin, the main bisisoquinoline alkaloid of *Stephania cepharantha*, has been limited to the alternatives (I) and (II).⁴¹ Ozonisation of the methin base gave 6-methoxydiphenyl



ether-3 : 4-dialdehyde and a dibasic dialdehyde, which on Hofmann degradation yielded trimethylamine and a divinyl-dialdehyde.

⁴⁰ An arrangement with one ethylenic linkage in ring *B* and a displacement of either the methyl or the acetamido-group to a neighbouring carbon atom would overcome this difficulty.

⁴¹ H. Kondo, Y. Yamashita, and I. Keimatsu, *J. Pharm. Soc. Japan*, 1934, **54**, 108; H. Kondo and I. Keimatsu, *ibid.*, 1935, **55**, 25, 63; *Ber.*, 1938, **71**, 2553.

The latter was reduced by catalytic and by Clemmensen methods to a diphenyl ether which was identical with a synthetic ether of structure (III). Cepharanthin is the first methylenedioxy-representative of the bisisoquinoline group, but attempted demethylenation led to profound decomposition and conversion into the trimethoxy-analogue, tetrandin or oxyacanthin *O*-methyl ether (see *Ann. Reports*, 1933, **30**, 246), was not realised.

(b) *Senecio and Heliotropium alkaloids* (see *Ann. Reports*, 1936, **33**, 377). The table includes some of the numerous alkaloids which have been isolated from *Senecio* and *Heliotropium* species, together with their alkaline hydrolysis products.

Alkaloid.	Products of hydrolysis.		Ref.
	Acid.	Base.	
Retrorsine, $C_{18}H_{23}O_4N$	Retronecic, $C_{10}H_{11}O_6$	Retronecine, $C_8H_{13}O_2N$	42, 43
Jacobine, $C_{18}H_{23}O_4N$	Jaconecic, $C_{10}H_{11}O_6$	" "	42, 44
Seneciophylline, $C_{18}H_{23}O_4N$	Seneciophyllic, $C_{10}H_{11}O_6$	" "	45
Senecionine, $C_{18}H_{23}O_4N$	Senecic, $C_{10}H_{11}O_6$	" "	46, 47
Platyphylline, $C_{18}H_{23}O_4N$	Platynecic, $C_{10}H_{11}O_6$	Platynecine, $C_8H_{13}O_2N$	48
Trichodesmine, $C_{18}H_{23}O_4N$	<i>dl</i> -Lactic acid and methyl isobutyl ketone	Retronecine, $C_8H_{13}O_2N$	49
Lasiocarpine, $C_{21}H_{29}O_7N$	Angelcic and lasiocarpic, $C_8H_{13}O_6$	Heliotridine, $C_8H_{13}O_2N$	50
Heliotrine, $C_{18}H_{23}O_4N$	Heliotric, $C_8H_{13}O_6$	" "	51

The first five alkaloids are derived from *Senecio* species, trichodesmine occurs in *Trichodesma incanum* and lasiocarpine and heliotrine were isolated from *Heliotropium lasiocarpin*. The *Senecio* bases contain eighteen atoms and yield on alkaline hydrolysis an acid containing ten carbon atoms and a dihydroxy-tertiary base, usually retronecine, containing eight carbon atoms. It has been shown that reduction of retronecine,⁵² platynecine⁴⁸ or heliotridine⁵³ yields the same product, $C_8H_{15}N$, known as heliotridan (II), and a relationship between the *Senecio* and the *Heliotropium* bases is therefore established. Reduction of the methin base of (I) gave a pyrrolidine derivative (II),⁵⁴ which was converted into the base

⁴² R. H. F. Manske, *Canadian J. Res.*, 1931, **5**, 654.

⁴³ G. Barger, T. R. Seshadri, H. E. Watt, and T. Yabuta, *J.*, 1935, 11.

⁴⁴ G. Barger and J. J. Blackie, *J.*, 1937, 584.

⁴⁵ R. A. Konovalova and A. P. Orékhof, *Bull. Soc. chim.*, 1937, **4**, 2037.

⁴⁶ G. Barger and J. J. Blackie, *J.*, 1936, 743.

⁴⁷ R. H. F. Manske, *Canadian J. Res.*, 1936, **14**, 8.

⁴⁸ R. A. Konovalova, *Bull. Acad. Sci. U.R.S.S.*, 1937, 961.

⁴⁹ G. P. Menschikov, *Ber.*, 1935, **68**, 2039.

⁵⁰ *Idem*, *ibid.*, p. 1110.

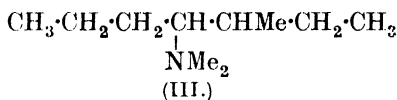
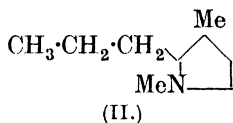
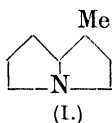
⁵¹ *Idem*, *Ber.*, 1932, **65**, 974.

⁵² L. Konovalova and A. P. Orékhof, *Bull. Soc. chim.*, 1937, **4**, 1285.

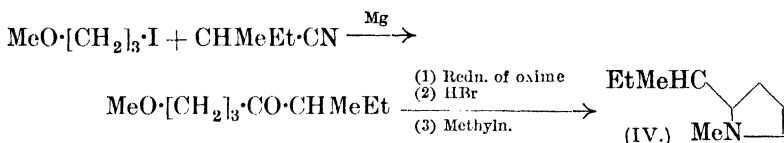
⁵³ G. P. Menschikov, *Ber.*, 1933, **66**, 875; 1935, **68**, 1051.

⁵⁴ *Idem*, *Ber.*, 1935, **68**, 1555.

(III) by Hofmann degradation and subsequent reduction.⁵⁵ This



tertiary base (III) was also obtained by reduction of the methin base prepared from (IV), which was synthesised as follows : ⁵⁶



The tertiary base (III) must be derived from either (II) or (IV) and, as the pyrrolidine derivative (II) differs from the synthetical base (IV), its structure and that of heliotridan (I) are established. A synthesis of *dl*-heliotridan has also been reported.⁵⁵ Consequently heliotrin and retronecine are monoethylenic dihydroxy-derivatives of (I) differing in orientation of the hydroxyl groups and/or ethylenic linkage, and platynecine corresponds to a saturated dihydroxy-derivative of (I).

The structures of the acids obtained by hydrolysis of the alkaloids are not settled. Although the majority contain ten carbon atoms, they exhibit great variation in structure. Aliphatic, cyclic, saturated and unsaturated representatives have been obtained, and hydroxyl, methoxyl, carbonyl and lactonic groups have been detected. The frequent occurrence of the C_{10} acids, the isolation of angelic acid from lasiocarpine, and the presence of *C*-methyl groups⁴⁶ suggest a terpenoid structure for the acids. In the alkaloids, the acidic fragment is combined by an ester linkage with the dihydroxy-base; in heliotrin and the *Senecio* bases one hydroxyl group only is esterified, but lasiocarpine and trichodesmine may contain two ester linkages.

R. D. H.

⁵⁵ G. P. Menschikov, *Bull. Acad. Sci. U.R.S.S.*, 1937, 1035.

⁵⁶ *Idem*, *J. Gen. Chem. Russia*, 1937, 7, 1632.

BIOCHEMISTRY.

ANIMAL BIOCHEMISTRY.

Introduction.

INVESTIGATIONS in biochemistry cover such a wide field that it can invariably be said, with truth, that considerable progress has been made.

As in past years, vitamins have been dealt with at some length : the progress is so marked that it is impossible to neglect the subject. In particular might be mentioned the identification and synthesis of vitamin E, the work on nicotinic acid, and the rapid advance in investigations on the other components of B₂ and on vitamin K. Valuable contributions to chemical methods for determining certain vitamins are discussed in another section. Subjects which have not received much attention, certainly during the past two years, include the hormones, enzymes,¹ the chemistry of micro-organisms,² carcinogenic substances,³ chemical changes in muscle, yeast metabolism, and biological oxidations and reductions; in all these fields important advances have been made. Amongst other subjects which offer special interest to biochemists are the proteins : this important field is adequately dealt with in another section of these Reports (p. 366).

The use of isotopes in the study of metabolism is in its infancy, but sufficient has already been accomplished to show that the method will prove of real value. The success of the chemical studies on heparin has led to important clinical applications, and the work done during the past year on sulphanilamide and related drugs has more than justified the statement made last year that the discovery of these drugs was " probably the most important advance in chemotherapy for many years."

The Vitamins.

The vitamin story may now be regarded as approaching the end of what is possibly the most important chapter, that dealing with

¹ Reviews of the recent work on several of the enzymes will be found in *Ergebn. Enzymforsch.*, 1938, **7**, and in earlier volumes.

² *E.g.*, the many papers by H. Raistrick and his colleagues (in the *Biochem. J.*, etc.); cf. also a chapter by H. Raistrick in " Perspectives in Biochemistry " (Camb. Univ. Press, 1937).

³ An interesting account of some of the recent work is given by E. C. Dodds (*Lancet*, 1938, **235**, 351).

the identification of those vitamins which are required for the prevention of certain widespread deficiency diseases in man. This statement does not suggest that those vitamins which have not yet succumbed to intensive chemical attack are not needed by man, nor does it mean that all the vitamins required by man have been discovered. The list of "recognised" vitamins five years hence will probably be considerably longer than the present-day list, but in view of the very general character of investigations on this subject it will be rather surprising if some serious vitamin deficiency disease has so far been missed. In dealing with the vitamins, experience has shown that it is unwise to make dogmatic statements about the number of possible vitamins, or to accept or discredit, without allowing sufficient time for an adequate test, any new observation. Furthermore, we must be prepared for discoveries showing that two or more closely related substances possess similar vitamin activities, as has already occurred with vitamins A, D and E.

The present-day knowledge of the chemical properties of the vitamins cannot be indicated more clearly than by a list of those vitamins which are now available as synthetic products. In this list are vitamin B₁, two members of the B₂-complex (riboflavin and nicotinic acid), C, E and possibly A. In addition, D is readily available commercially as a crystalline product and crystalline B₆ (another member of the B₂-complex) has recently been isolated.

Perhaps one of the most valuable publications on vitamins during the past year is the first volume of a series of monographs by L. J. Harris.⁴

*Vitamin A (Axerophthol)*⁵.—The nature and distribution of the suggested second factor (A₂) has aroused considerable interest. J. R. Edisbury, R. A. Morton, G. W. Simpkins, and J. A. Lovern⁶ have determined the vitamin A content of various tissues of rabbits and many kinds of fish, and have attempted to correlate the results with possible functions of this vitamin; as yet, no definite conclusions as to the participation of the vitamin in fat exchange or assimilation can be reached. Factor A₂ tends to replace vitamin A in freshwater fish, but does not seem to occur in mammals. Similar studies on Russian fish have been made by A. E. Gillam, I. M. Heilbron, W. E. Jones, and E. Lederer,⁷ who have also tried to separate and identify the 6930 Å. chromogen (A₂). Although this attempt was not successful, they obtained evidence that this factor

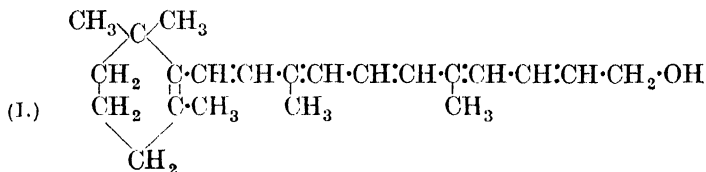
⁴ "Vitamins and Vitamin Deficiencies." Vol. 1. Historical and Introductory. Vitamin B₁ and Beri-beri. L. J. Harris (J. and A. Churchill), 1938.

⁵ The name suggested by P. Karrer (cf. H. v. Euler, P. Karrer, and U. Solmssen, *Helv. Chim. Acta*, 1938, **21**, 211).

⁶ *Biochem. J.*, 1938, **32**, 118.

⁷ *Ibid.*, p. 405.

is the C_{22} homologue of vitamin A, with six ethylenic linkages. They suggest formula (I) for factor A_2 .⁸



Biological tests suggest that A_2 contributes to the total vitamin A activity of A-concentrates, but more extensive investigation will be needed before this factor is accepted as vitamin A_2 .⁸ E. Lederer and F. H. Rathmann⁹ have shown that A_2 gives with antimony trichloride a second absorption band at 6500 Å. and that with concentrates rich in A_2 nearly half the absorption at 6200 Å. is due to overlapping, necessitating a redetermination of the A_1/A_2 ratios. These authors have also shown that the rat and frog can absorb A_2 from the intestine and can accumulate it in the liver. A_2 appears to be, therefore, a specific product of the liver metabolism of certain species of freshwater fish, and its absence from the liver of mammals can be attributed to its absence from their food. This conclusion receives support from the investigations of A. E. Gillam,¹⁰ who has shown that A_2 is absent from the livers of mammals and birds, but present in the livers of animals known to feed on fish, and in the liver of a rat fed with a concentrate containing A_2 . Up to the present, therefore, there is no indication that A_2 , although it might have a biological value equal to A_1 , plays any significant rôle in mammalian nutrition.

T. Thorbjarnarson and J. C. Drummond¹¹ have found that the storage of vitamin A in the liver is facilitated by the presence of fat in the diet. The administration of choline, which prevents deposition of liver-fat, causes a low storage of vitamin A. Fat leaving the liver may take vitamin A with it, but the retention of fat does not necessarily mean the retention of the vitamin. The administration of large doses of A to rats and guinea-pigs causes no symptoms of true hypervitaminosis according to I. Ikegaki,¹² and

⁸ The results of H. v. Euler, P. Karrer, and U. Solmssen (*Helv. Chim. Acta*, 1938, **21**, 211) and of P. Karrer, A. Rüegger, and A. Geiger (*ibid.*, p. 1171) suggest, however, that some modification of this formula may be necessary. With Karrer's classification, formula (I) represents β -apo-5-carotinol.

⁹ *Compt. rend.*, 1938, **206**, 781; *Biochem. J.*, 1938, **32**, 1252.

¹⁰ *Biochem. J.*, 1938, **32**, 1496.

¹¹ *Ibid.*, p. 5.

¹² *Z. Vitaminforsch.*, 1938, **7**, 113.

the vitamin is only toxic to rats if given in doses in excess of 100,000 I.U. per day.¹³

Several investigators have studied the prevalence of vitamin A-deficiency in man, using methods which vary from the determination of the vitamin in the serum and urine to a measurement of dark adaptation. The last-named method is based on the finding that individuals who have a partial or complete deficiency of this vitamin show some degree of "night-blindness" after exposure to bright light, and several modifications of the original method of P. C. Jeans and Z. Zentmire¹⁴ have been described. Most of the investigations have reported a considerable amount of vitamin A-deficiency amongst the poorer populations even in the countries where the standard of nutrition is supposed to be high. M. K. Maitra and L. J. Harris¹⁵ have shown, for example, that 22—36% of elementary school-children in the east of London and in Cambridge were in the "definitely subnormal" group, whereas none of the boys at a public school was in this category. When treated with vitamin A for four weeks, 39 out of 40 in the former group became normal or showed improvement, whereas untreated controls remained subnormal. H. Jeghers¹⁶ has found partial vitamin A-deficiency not uncommon in adults, and several other authors have reported on this method and the results of their surveys.¹⁷

Crystalline anthraquinone-2-carboxylic and 2-naphthoic esters of vitamin A, prepared by T. H. Mead,¹⁸ have been tested biologically by K. H. Coward and S. W. F. Underhill.¹⁹ From the potency of these esters, the potency of vitamin A alcohol is calculated to be 3.32×10^6 I.U. per g., i.e., twice the activity of the international standard of β -carotene (1.667×10^6 units per g.). These results suggest that one molecule of β -carotene is converted into one molecule of vitamin A in the animal body, and not two as has generally been supposed.

Vitamin B₁ (Aneurin or Thiamin).—Interesting accounts of the chemistry and the biological significance of this vitamin are given by

¹³ E. B. Vedder and C. Rosenberg, *J. Nutrition*, 1938, **16**, 57.

¹⁴ *J. Amer. Med. Assoc.*, 1934, **102**, 892; cf. also P. C. Jeans, E. Blanchard, and Z. Zentmire, *ibid.*, 1937, **108**, 451.

¹⁵ *Lancet*, 1937, **233**, 1009; cf. also M. A. Abbasy and L. J. Harris, *Chem. and Ind.*, 1938, **57**, 86; B. Ahmad and L. J. Harris, *ibid.*, p. 1190.

¹⁶ *Ann. Intern. Med.*, 1937, **10**, 1304; *J. Amer. Med. Assoc.*, 1937, **109**, 756.

¹⁷ J. R. Mutch and H. D. Griffith, *Brit. Med. J.*, 1937, **ii**, 565; B. L. Isaacs, F. T. Jung, and A. C. Ivy, *J. Amer. Med. Assoc.*, 1938, **111**, 777; C. Schuck and W. O. Miller, *Arch. Intern. Med.*, 1938, **61**, 910; N. T. Gridgeman and H. Wilkinson, *Lancet*, 1938, **234**, 905; C. E. Palmer, *Amer. J. Publ. Health*, 1938, **28**, 309.

¹⁸ *Chem. and Ind.*, 1938, **57**, 1189.

¹⁹ *Ibid.*, p. 1189.

R. R. Williams,²⁰ whose brilliant work leading to the establishment of the formula and to the synthesis of this vitamin has been dealt with in previous Reports. These papers and the very comprehensive review by L. J. Harris⁴ will furnish the most exacting reader with a full account of the work on the anti-neuritic vitamin up to about the middle of 1938, and will indicate the trend of modern views on the relationship between this vitamin and various enzymic systems concerned with carbohydrate metabolism. The full fruition of the chemical attacks on B₁ appears to be indicated by the recent adoption of crystalline vitamin B₁ hydrochloride as the international standard, in place of the adsorbate hitherto used.

The study of the relationship between B₁ and co-carboxylase, stimulated by the recognition of the latter as the pyrophosphoric ester of vitamin B₁,²¹ has been continued by many investigators. The synthesis of co-carboxylase from the vitamin by the action of yeast, animal tissues or by simple chemical processes is effected quite readily,²² and there is much support for the view that in the animal body vitamin B₁ may play a rôle similar to that of co-carboxylase in yeast.²³ The conversion of the vitamin into co-carboxylase by liver slices or "brei" is at an optimum at about *p*_H 8.5 and the synthesis is inhibited by iodoacetic acid but is little affected by fluoride.²⁴ The results of S. Ochoa and R. A. Peters²⁵ confirm the view that co-carboxylase is a very significant form of vitamin B₁ in animal tissues; in some, such as brain and liver, it appears to be predominant. These authors find that the administration of B₁ leads to an immediate accumulation of both B₁ and its pyrophosphoric ester in the liver, and they make the interesting observation that this is the first time that the liver has been brought into prominence in the metabolism of this vitamin.

The importance of the vitamin in carbohydrate metabolism as a component of the pyruvic acid oxidation system is fully reviewed by R. A. Peters,²⁶ and B. S. Platt²⁷ gives an account of the studies

²⁰ *Science*, 1938, **87**, 559; *J. Amer. Med. Assoc.*, 1938, **110**, 727.

²¹ K. Lohmann and P. Schuster, *Naturwiss.*, 1937, **25**, 26; *Biochem. Z.*, 1937, **294**, 188.

²² H. W. Kinnersley and R. A. Peters, *Chem. and Ind.*, 1937, **56**, 447; H. von Euler and R. Vestin, *Naturwiss.*, 1937, **25**, 416; H. Tauber, *Science*, 1937, **86**, 180; *J. Amer. Chem. Soc.*, 1938, **60**, 730; *J. Biol. Chem.*, 1938, **123**, 499; **125**, 191; M. A. Lipschitz, V. R. Potter, and C. A. Elvehjem, *Biochem. J.*, 1938, **32**, 474; H. W. Kinnersley and R. A. Peters, *ibid.*, p. 697.

²³ Cf. discussion by L. J. Harris, ref. (4).

²⁴ S. Ochoa and R. A. Peters, *Nature*, 1938, **142**, 356.

²⁵ *Chem. and Ind.*, 1938, **57**, 471; *Biochem. J.*, 1938, **32**, 1501.

²⁶ *Trans. Roy. Soc. Trop. Med. Hyg.*, 1938, **31**, 483.

²⁷ *Ibid.*, p. 493.

which have shown that in beri-beri there is an increase in the blood pyruvic acid. The action of the vitamin is not confined to carbohydrate metabolism, but also concerns fat metabolism, possibly by an indirect process. E. W. McHenry²⁸ has shown, for example, that B₁ and choline have a complementary effect in increasing the weights of young rats, and that B₁ administered to rats maintained on a low-choline diet causes a marked increase in liver fat. In the rat and pigeon, B₁ causes fat formation from carbohydrate, apparently in the liver, and subsequently choline, flavin and B₆ promote fat migration from the liver to the depots.²⁹

Several authors have made determinations of the amount of vitamin B₁ in the serum or the urine, and have attempted to assess the clinical significance of the results. E. N. Rowlands and J. F. Wilkinson³⁰ have, for example, used a modification of the method of W. H. Schopfer³¹ (which involves the use of *Phycomyces blakesleeanus*) for determining the blood vitamin B₁, and have reported gross deficiencies in alcoholic neuritis, nutritional neuritis, scurvy and "malnutrition." L. J. Harris, P. C. Leong, and C. C. Ungley³² have continued their study of the excretion of B₁ in the urine, as determined by the "bradycardia" method, and conclude that the urinary excretion furnishes a useful guide to the state of nutrition of the subject with regard to this vitamin. These authors have also alluded to "conditioned deficiency" of vitamin B₁ as a cause of polyneuritis in various diseases, such conditioned deficiency being diagnosed by urine tests. A carbohydrate-tolerance test for B₁ has recently been devised by G. G. Banerji and L. J. Harris,³³ and it seems possible that this test may be of considerable value for surveys of the level of nutrition of large groups of the population.

Vitamin B₂-Complex.—Several vitamins of the B-group have been discovered in recent years, and much confusion has arisen, and still exists, with regard to the nomenclature. Following the separation and identification of B₁, the other members of this ill-assorted family have been given various designations. Least confusion is probably caused when the term B₂ is used for the B group minus B₁. Under this classification there are now at least four

²⁸ *Biochem. J.*, 1937, **31**, 1616; *J. Physiol.*, 1937, **89**, 287; *Science*, 1937, **86**, 200.

²⁹ Private communication from Dr. E. W. McHenry.

³⁰ *Brit. Med. J.*, 1938, ii, 878, 1110; cf., however, criticism by H. M. Sinclair, *ibid.*, pp. 1060, 1111.

³¹ Cf. *Ann. Reports*, 1937, **34**, 401.

³² *Lancet*, 1938, **234**, 539. For the other literature on this subject, see ref. (4).

³³ *Chem. and Ind.*, 1938, **57**, 1190.

different well-characterised vitamins, of which the first two have been identified and synthesised :

- (1) Riboflavin (a more satisfactory name than lactoflavin).
- (2) Nicotinic acid (the pellagra-preventing or anti-black-tongue factor).
- (3) Vitamin B₆ (the rat-dermatitis preventing factor).
- (4) The chick-antidermatitis factor.

The filtrate factor³⁴ may be identical with (4) and the yeast eluate factor with B₆,³⁵ but the above list is probably by no means complete. Pigeons require factors which have been designated B₃ and B₅ (though these may not differ from the "recognised" components of the B₂-complex), and certain animal species may need factors other than those listed above. Little is known, however, about the chemical properties of these additional factors.

The discovery, reported last year, that nicotinic acid or nicotinamide will cure black-tongue in dogs³⁶ and pellagra in man,³⁷ has been followed by many confirmatory reports.³⁸ Spectacular results follow the administration, orally or by injection, of nicotinic acid or nicotinamide to patients suffering from pellagra, and similar treatment cures pellagra in monkeys³⁹ or in pigs.⁴⁰ The dramatic results which follow the addition of 60 mg. of nicotinic acid daily for three months to the diet of pigs suffering from pig-dermatitis are beautifully shown in photographs presented by H. Chick, T. F. Macrae, A. J. P. Martin, and C. J. Martin.⁴⁰

The observation⁴¹ that nicotinic acid (or some substance which gives a similar colour reaction) is absent from the urine of pellagrins,

³⁴ Cf. *Ann. Reports*, 1937, **34**, 404.

³⁵ C. E. Edgar, M. M. El Sadr, and T. F. Macrae, *Chem. and Ind.*, 1938, **57**, 1111; *Biochem. J.*, 1938, **32**, 2200.

³⁶ C. A. Elvehjem, R. J. Madden, F. M. Strong, and D. W. Woolley, *J. Amer. Chem. Soc.*, 1937, **59**, 1767; *J. Biol. Chem.*, 1938, **123**, 137; cf. also W. J. Dann and Y. Subbarow, *J. Nutrition*, 1938, **16**, 183.

³⁷ P. J. Fouts, O. M. Helmer, S. Lepkovsky, and T. H. Jukes, *Proc. Soc. Exp. Biol. Med.*, 1937, **37**, 405; L. J. Harris and A. Hassan, *Nature*, 1937, **140**, 1070; D. T. Smith, J. M. Ruffin, and S. G. Smith, *J. Amer. Med. Assoc.*, 1937, **109**, 2054.

³⁸ T. D. Spies, *Lancet*, 1938, **234**, 252; T. D. Spies, C. Cooper, and M. A. Blankenhorn, *J. Amer. Med. Assoc.*, 1938, **110**, 622; T. D. Spies, W. B. Bean, and R. E. Stone, *ibid.*, 1938, **111**, 584 (who report that "they have not observed a case of acute pellagra which has not responded promptly to nicotinic acid"); cf. also ref. (42); R. S. Mathews, *ibid.*, p. 1148; A. C. Alport, P. Ghalioungui, and G. Hanna, *Lancet*, 1938, **235**, 1460.

³⁹ L. J. Harris, *Nature*, 1937, **140**, 1070; *Biochem. J.*, 1938, **32**, 1479.

⁴⁰ *Ibid.*, pp. 10, 844.

⁴¹ S. P. Vilter, T. D. Spies, and A. P. Mathews, *J. Amer. Chem. Soc.*, 1938, **60**, 731.

but is excreted by normal individuals, and by pellagrins who receive nicotinic acid or amide, may be taken as support, if this is needed, for the view that pellagra is associated with a deficiency of this acid. As a potent therapeutic agent for treatment of pellagra, nicotinic acid is certain to be of inestimable value, but there can be no doubt that pellagra-producing diets must often be deficient in a number of other substances.⁴² Furthermore, it is generally agreed that where the diet contains a reasonable proportion of dairy produce and meat, there is no pellagra, and, to quote the words of J. C. Drummond,⁴³ this problem "is not a question of nicotinic acid; it is simply one of £. s. d."

Many authors have tested the pellagra or black-tongue curing powers of substances related to nicotinic acid. β -Aminopyridine is ineffective,⁴⁴ and it appears probable that only those pyridine derivatives which are capable of oxidative or hydrolytic conversion into nicotinic acid (or amide) in the body are active in this respect.⁴⁵

Vitamin B₆ (for which the name adermin has been suggested) has recently been obtained crystalline⁴⁶ and has been given the empirical formula C₈H₁₂O₃NCl. The chick antidermatitis factor is acidic and contains one or more hydroxyl or amino-groups.⁴⁷

Vitamin C (Ascorbic Acid).—The urinary excretion of this vitamin by the normal individual and by patients suffering from various diseases has been studied by many authors. Although the suggestion that there may be a relationship between a deficiency of this vitamin and an increased tendency to certain infections⁴⁸ has been the subject of criticism,⁴⁹ there is a considerable amount of evidence that in some infections the ascorbic acid excretion is subnormal and that the patients are "unsaturated" with regard to this vitamin.

⁴² Cf. J. M. Grant, E. Zschiesche, and T. D. Spies, *Lancet*, 1938, **234**, 939.

⁴³ In a preface to "Science and Nutrition," A. L. Bacharach (Watts and Co.), London, 1938.

⁴⁴ F. M. Strong, R. J. Madden, and C. A. Elvehjem, *J. Amer. Chem. Soc.*, 1938, **60**, 2564; Y. Subbarow and W. J. Dann, *ibid.*, p. 2565. β -Aminopyridine is also without action in monkey pellagra (private communication from Dr. L. J. Harris).

⁴⁵ D. W. Woolley, F. M. Strong, R. J. Madden, and C. A. Elvehjem, *J. Biol. Chem.*, 1938, **124**, 715.

⁴⁶ P. György, *J. Amer. Chem. Soc.*, 1938, **60**, 983; R. Kuhn and G. Wendt, *Ber.*, 1938, **71**, 780, 1118; J. C. Keresztesy and J. R. Stevens, *J. Amer. Chem. Soc.*, 1938, **60**, 1267; A. Ichiba and K. Michi (cited from P. W. Wiardi, *Nature*, 1938, **142**, 1158).

⁴⁷ D. W. Woolley, H. A. Waisman, O. Mickelsen, and C. A. Elvehjem, *J. Biol. Chem.*, 1938, **125**, 715.

⁴⁸ Cf. *Ann. Reports*, 1937, **34**, 407.

⁴⁹ Cf. review by L. G. Parsons, *Lancet*, 1938, **234**, 123.

In diseases such as pulmonary tuberculosis, osteomyelitis, rheumatoid arthritis, rheumatic fever, whooping cough and sometimes in diabetes there is often a hypovitaminosis C, as shown by a diminished urinary excretion and a delay in the excretion of ascorbic acid added to the diet. Whether this deficiency is due to an increased rate of metabolism concurrent with the pyrexia, a deficiency in the diet, a lowered renal threshold (to account for the low plasma-ascorbic acid), a decreased absorption of the vitamin, an increased utilisation of the vitamin by the leucocytes and other cells, or to some cause unrelated to the infection, there appears to be justification for the addition of suitable sources of vitamin C to patients suffering from, and convalescing after, diseases of this type.

The possible significance of ascorbic acid in immunological reactions has received much attention, but the reports made are often of a conflicting nature. It is perhaps too early to attempt to reach any definite conclusions as to any possible antitoxic action of the vitamin, the alleged protective action against anaphylactic shock, or the reported stimulation, by the vitamin, of specific antibody production. The view that vitamin C has a protective action against diphtheria toxin has, however, been contested by S. S. Zilva.⁵⁰

Vitamin E (α -, β - and γ -Tocopherols).—This vitamin has now succumbed to the intensive chemical attack made by investigators in several laboratories, and work carried out during the past twelve months has added the last chapter to its story. There is now almost unanimous agreement as to the structure of α - and β -tocopherols ($C_{29}H_{50}O_2$ and $C_{28}H_{48}O_2$ respectively), two substances with vitamin E activity which can be separated from the oils of wheat-germ, rice-germ and cotton-seed. The fertility of vitamin E-deficient rats is restored by the addition of 3 mg. of the α -compound or 5 mg. of the β -compound to the diet.⁵¹

The observation of E. Fernholz⁵² that α -tocopherol yields duroquinol when heated and the similar work of W. John⁵³ have been followed by the suggestion, made independently and practically simultaneously by four groups of workers, that the tocopherols are coumarans or chromans with side chains.⁵⁴ Synthesis of α -toco-

⁵⁰ *Brit. J. Exp. Path.*, 1937, **18**, 449.

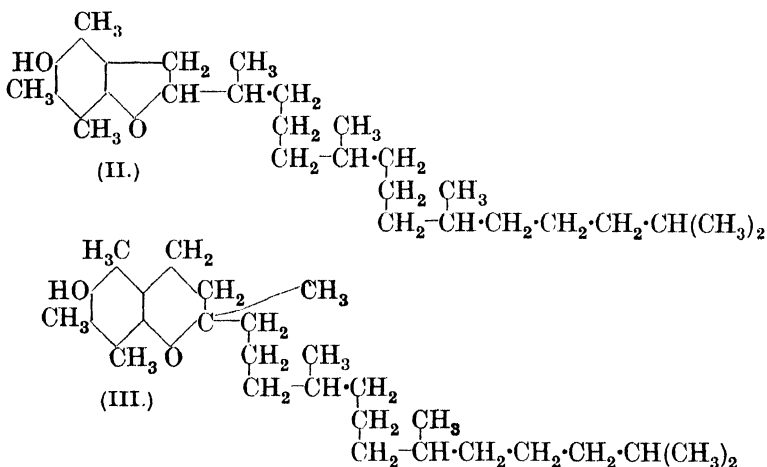
⁵¹ A. L. Bacharach (*Nature*, 1938, **142**, 35), using the purified allophanates, records 1.2 and 1.9 mg. for the mean fertility doses of α - and β -tocopherol respectively for rats.

⁵² *J. Amer. Chem. Soc.*, 1937, **59**, 1154.

⁵³ *Z. physiol. Chem.*, 1937, **250**, 11.

⁵⁴ E. Fernholz, *J. Amer. Chem. Soc.*, 1938, **60**, 700; W. John, *Z. physiol. Chem.*, 1938, **252**, 222; F. Bergel, A. R. Todd, and T. S. Work, *J.*, 1938, 253; F. Bergel, A. Jacob, A. R. Todd, and T. S. Work, *Nature*, 1938, **141**, 646; P. Karrer, H. Salomon, and H. Fritzsche, *Helv. Chim. Acta*, 1938, **21**, 309.

pherol has been effected by different methods by P. Karrer, H. Fritzsche, B. H. Ringier, and H. Salomon,⁵⁵ F. Bergel, A. Jacob, A. R. Todd, and T. S. Work,⁵⁶ and L. I. Smith, H. E. Ungnade, and W. W. Prichard,⁵⁷ and the products shown to be identical, in chemical and biological tests, with the natural product.⁵⁸ From this evidence α -tocopherol was given formula (II) or (III), *i.e.*, it has a coumaran or chroman structure, but it is now generally accepted that the chroman structure (III) is the correct one.



β -Tocopherol differs from the α -compound in having only two methyl groups in the aromatic nucleus, and F. Bergel, A. M. Copping, A. Jacob, A. R. Todd, and T. S. Work⁵⁹ have recently obtained a synthetic product, from *m*-xyloquinol and phytol, which appears to be isomeric or identical with β -tocopherol.⁶⁰ The pure tocopherols isolated from wheat-germ-oil, etc., account for only a fraction of the total vitamin E activity of the oil. This may be

⁵⁵ *Helv. Chim. Acta.*, 1938, **21**, 520, 820; *Nature*, 1938, **141**, 1057; P. Karrer and V. Demole, *Schweiz. med. Woch.*, 1938, **68**, 954.

⁵⁶ *Nature*, 1938, **142**, 36.

⁵⁷ *Science*, 1938, **88**, 37.

⁵⁸ The biological tests on the product obtained by Smith and his colleagues were made by H. M. Evans, G. A. Emerson, and O. H. Emerson (*Science*, 1938, **88**, 38).

⁵⁹ *J.*, 1938, 1382.

⁶⁰ The positions of the two methyl groups in the aromatic nucleus of β -tocopherol have not yet been established. In addition to the isomer mentioned, the other two have now been synthesised, from phytol and *o*- and *p*-xyloquinol, and found to have about the same activity as β -tocopherol (private communication from Prof. A. R. Todd). P. Karrer and H. Fritzsche (*Helv. Chim. Acta*, 1938, **21**, 1234) have also recently synthesised the three possible β -tocopherols, and found all three active.

due to loss during the preparation or to the existence of other tocopherols or related compounds with anti-sterility properties, and in this connection it would be useful to have more information about γ -tocopherol, which according to O. H. Emerson, G. A. Emerson, A. Mohammad, and H. M. Evans ⁶¹ has an activity about one-half or one-third that of α -tocopherol.

The considerable loss of vitamin E during saponification is referred to by A. R. Moss and J. C. Drummond, ⁶² who have recently described a new method for the isolation of α - and β -tocopherols, involving adsorption by alumina from solution in light petroleum; by this method, 2 kg. of wheat-germ oil yielded 1 g. of α -tocopherol allophanate and 0.75 g. of β -tocopherol allophanate.

Space will not permit a description of the recent work on the physiological activity of vitamin E, but if this were possible, little could be added to the excellent account given by A. L. Bacharach. ⁶³ This author reviews the subject of the relationship between vitamin E and the gonads and the anterior pituitary, and investigations dealing with the use of the vitamin in the treatment of sterility in women and for veterinary purposes. The same author and his colleagues ⁶⁴ have made valuable contributions in connection with the biological assay of this vitamin, and the relationship between dosage and response to vitamin E. ⁶⁵

Vitamin K.—Satisfactory evidence of a true vitamin deficiency in chickens, leading to a lengthening of the blood-clotting time, was presented in 1935 by H. Dam ⁶⁶ and independently by H. J. Almquist and E. L. R. Stokstad. ⁶⁷ An account of this work and some of the earlier observations which led to the recognition of vitamin K were given in these Reports for 1936. ⁶⁸ This fat-soluble vitamin is found in green leafy tissue (alfalfa, cabbage, spinach, etc.) and in moderate amounts in tomato, hempseed and soya-bean

⁶¹ *J. Biol. Chem.*, 1937—8, **122**, 99.

⁶² *Biochem. J.*, 1938, **32**, 1953. A similar method was previously described in an I. G. Patent (see footnote to this paper by A. R. Moss and J. C. Drummond).

⁶³ *Nutrit. Abs. Rev.*, 1938, **7**, 811; cf. also H. A. Mattill, *J. Amer. Med. Assoc.*, 1938, **110**, 1831. For work on the effect of vitamin E deficiency on the length of gestation and on lactation, see M. M. O. Barrie (*Biochem. J.*, 1938, **32**, 1467, 1474).

⁶⁴ A. L. Bacharach, E. Allchorne, and H. E. Glynn, *Biochem. J.*, 1937, **31**, 2287; A. L. Bacharach, *Nature*, 1938, **142**, 35, 875; A. L. Bacharach and E. Allchorne, *Biochem. J.*, 1938, **32**, 1298; cf. also K. E. Mason and W. L. Bryan, *ibid.*, p. 1785.

⁶⁵ A. L. Bacharach, *ibid.*, p. 2017.

⁶⁶ *Nature*, 1935, **135**, 652; *Biochem. J.*, 1935, **29**, 1273.

⁶⁷ *Nature*, 1935, **136**, 31; *J. Biol. Chem.*, 1935, **111**, 105.

⁶⁸ *Ann. Reports*, 1936, **33**, 394.

oil.⁶⁹ Hog-liver fat is a good source, but the liver of normal chicks contains very little.⁷⁰ A deficiency of the vitamin in the diet of chickens leads to subcutaneous and intramuscular hæmorrhage, with prolongation of the clotting time of the blood. Intravenous injection of the vitamin restores the clotting time to normal within 4—6 hours,⁷¹ but the vitamin has no *in vitro* action on blood from K-avitaminous chicks. The ingestion of large doses does not render the coagulability of the blood "supernormal."⁷² The precise rôle of the vitamin in the blood-clotting mechanism is at present not known, but the view that it is a component of prothrombin will probably have to be abandoned, since it has been shown that prothrombin preparations may have little vitamin K activity.⁷¹ Erosions and lesions of the chick gizzard lining have been associated with K-deficiency, but more recent work has shown that this defect is related to a deficiency of certain components of the bile, notably cholic acid.⁷³

Considerable progress has been made during the past two years by H. J. Almquist and by H. Dam and their colleagues in efforts to isolate the pure vitamin. Highly active concentrates are viscous oils, though a colourless crystalline solid has been obtained at low temperature,⁷⁴ and more recently S. A. Thayer, D. W. Mac-Corquodale, S. B. Binkley, and E. A. Doisy⁷⁵ claim to have isolated the vitamin as a crystalline solid, m. p. 69°. The chemical and physical properties of this vitamin have been summarised recently by A. A. Klose, H. J. Almquist, and E. Mecchi,⁷⁶ who conclude that they are consistent with those of a complex low-melting unsaturated hydrocarbon containing an aromatic grouping. The rapid progress made, and the recent improvements effected in the assay of the vitamin,⁷⁷ leave little doubt that the structure of this substance (or substances) will soon be elucidated.

The significance of the vitamin for mammals is not so clearly established, but H. Dam and J. Glavind⁷⁸ report a mild K-avi-

⁶⁹ For a list of the principal sources of this vitamin see refs. (66) and (67), and H. Dam and J. Glavind, *Biochem. J.*, 1938, **32**, 485.

⁷⁰ H. J. Almquist and E. L. R. Stokstad, *J. Nutrition*, 1936, **12**, 329.

⁷¹ H. Dam, J. Glavind, L. Lewis, and E. Tage-Hansen, *Skand. Arch. Physiol.*, 1938, **79**, 121.

⁷² H. Dam and J. Glavind, *Biochem. J.*, 1938, **32**, 1018.

⁷³ For a fuller description of this work, see H. J. Almquist, *Science*, 1938, **87**, 538; H. J. Almquist and E. Mecchi, *J. Biol. Chem.*, 1938, **126**, 407.

⁷⁴ H. J. Almquist, *Nature*, 1937, **140**, 25; *J. Biol. Chem.*, 1937, **120**, 635.

⁷⁵ *Science*, 1938, **88**, 243.

⁷⁶ *J. Biol. Chem.*, 1938, **125**, 681.

⁷⁷ H. Dam and J. Glavind, *Biochem. J.*, 1938, **32**, 1018; H. J. Almquist, E. Mecchi, and A. A. Klose, *ibid.*, p. 1897.

⁷⁸ *Acta Med. Scand.*, 1938, **96**, 108.

taminosis in rabbits. Interesting and promising results have been obtained in clinical tests on man, for a marked reduction in the clotting time of the blood of patients with obstructive jaundice has been observed following the injection of emulsions of vitamin K.⁷⁹ The suggestion has been made that treatment of this condition with the vitamin may completely replace the old bile therapy.⁸⁰

Vitamin P.—About two years ago, A. Szent-Györgyi and his colleagues⁸¹ suggested that fruit juices, Hungarian red pepper, etc., contain a substance (which they called vitamin P) which regulates the permeability of the capillaries, and they suggested that experimental scurvy, as in the guinea-pig, is a deficiency disease caused by the combined lack of vitamins C and P. From the results of chemical investigations these authors suggested that the vitamin is a flavone or flavonol glucoside ("citrin") and later that the crystalline substance hesperidin has vitamin P activity in guinea-pigs. Clinical trials with patients suffering from various diseases in which there is a low capillary resistance, gave promising results.

S. S. Zilva⁸² has made exhaustive efforts to confirm these findings with guinea-pigs, but finds that neither citrin nor hesperidin will delay the onset of scurvy or the fatal termination of the disease in these animals on a scorbutic diet; post-mortem examination revealed extensive fresh hæmorrhages. Zilva also found that a condition similar to that reported by Szent-Györgyi could be obtained simply by giving suboptimal doses of vitamin C. Th. Moll⁸³ also has obtained negative results, and at the present time unequivocal experimental proof of a deficiency disease due to a dietary deficiency of a vitamin P is lacking. The possibility that "citrin" preparations and nearly pure hesperidin may contain some closely related substance which is the active agent⁸⁴ could account for some but not all of these discrepancies.

Therapeutic tests with hesperidin or "citrin" have sometimes given promising results and several authors⁸⁵ have reported satisfactory results following the administration of these preparations by mouth, or by injection, to patients suffering from certain diseases in which there is an increased permeability of the capillaries. The

⁷⁹ H. Dam and J. Glavind, refs. (78) and (80).

⁸⁰ *Idem*, *Lancet*, 1938, **234**, 720.

⁸¹ For the references, see ref. (82).

⁸² *Biochem. J.*, 1937, **31**, 915, 1488; *Nature*, 1937, **140**, 588.

⁸³ *Klin. Woch.*, 1937, **16**, 1653.

⁸⁴ Cf. H. Lotze, *Deutsche med. Woch.*, 1938, **64**, 477.

⁸⁵ S. Ruzsnyák and A. Szent-Györgyi, *Nature*, 1936, **138**, 27; S. Lajos, *Klin. Woch.*, 1937, **16**, 1615; T. Jersild, *Lancet*, 1938, **234**, 1445; H. Scarborough and C. P. Stewart, *ibid.*, **235**, 610.

position with regard to vitamin P is, however, still obscure. The failure of other workers to confirm, with animals, the original observations of A. Szent-Györgyi, and the absence of large-scale well-controlled clinical tests, suggest that the time has not yet arrived for the full recognition of vitamin P.

Insulin, Diabetes and the Glycotropic Factor of the Anterior Pituitary.

The chemistry of insulin has been dealt with briefly at various times in these Reports,⁸⁶ but this is perhaps a convenient opportunity to review the progress made. By the use of various inactivating agents, considerable progress has been made in determining groups which may be concerned with the activity of this hormone, and many investigators have undoubtedly visualised the possibility of synthesising some relatively simple compound possessing these active groups and having a hypoglycaemic power similar to that of insulin. In the most optimistic dreams these insulin-substitutes have been resistant to the action of proteolytic enzymes and have therefore been effective when given by mouth. These dreams have not yet materialised.

The chemical attack on insulin has been made by numerous authors, including K. Freudenberg,⁸⁷ C. R. Harington,⁸⁸ H. Jensen,⁸⁹ D. A. Scott⁹⁰ and O. Wintersteiner⁹⁰ and their colleagues and many others.⁹¹ The hormone is inactivated by a variety of agents, including proteolytic enzymes, alkalis, acid-alcohol, cysteine, glutathione, ascorbic acid, iodine, acetic anhydride, formaldehyde, phenyl isocyanate, benzyl chloroformate, and keten; in some instances the loss of hypoglycaemic power can be attributed to a definite change in part of the protein molecule. So far there is

⁸⁶ *Ann. Reports*, 1936, **33**, 396; 1937, **34**, 309.

⁸⁷ K. Freudenberg and various colleagues, *Z. physiol. Chem.*, 1928, **175**, 1; 1929, **180**, 212; 1930, **187**, 89; 1931, **202**, 97, 128, 159, 192; 1932, **204**, 233; **213**, 226, 248; 1935, **233**, 159; cf. review by K. Freudenberg, *Monatsh.*, 1936, **69**, 144.

⁸⁸ C. R. Harington and A. Neuberger, *Biochem. J.*, 1936, **30**, 809; C. R. Harington and T. H. Mead, *ibid.*, p. 1598.

⁸⁹ For the earlier papers, see H. Jensen and E. A. Evans, *Physiol. Rev.*, 1934, **14**, 188; cf. also *J. Biol. Chem.*, 1935, **108**, 1; H. Jensen, E. A. Evans, W. D. Pennington, and E. D. Schock, *ibid.*, 1936, **114**, 199.

⁹⁰ Cf. review by H. Jensen and E. A. Evans, ref. (89). For other work on the chemistry of insulin, see K. G. Stern and A. White, *J. Biol. Chem.*, 1937, **117**, 95; 1938, **122**, 371; A. White and K. G. Stern, *ibid.*, 1937, **119**, 215.

⁹¹ D. W. Hill and F. O. Howitt ("Insulin. Its Production, Purification and Physiological Action." Hutchinson's Scientific and Technical Publications. London, 1936) and H. F. Jensen ("Insulin. Its Chemistry and Physiology." The Commonwealth Fund. New York, 1938) give full reviews of this literature.

evidence that changes in the S-S groups, in the tyrosine (*e.g.*, the introduction of two iodine atoms *ortho* to the hydroxyl group), and possibly in the free amino-groups, cause loss of activity. In a few cases, reactivation of the inactive product can be effected by removal of the new groups or by a reversal of the chemical change which causes inactivation. Up to the present, however, these observations have not rendered possible the preparation of a simpler or synthetic insulin, but the evidence which has accrued may some day help to solve the problem as to the exact function of this hormone in carbohydrate metabolism.

In another direction much progress has been made in the past two or three years. This refers to the preparation of insulin derivatives which, after injection into the body, exert their activity for a longer period than does ordinary insulin. The outstanding success in these efforts was attained in 1936 by H. C. Hagedorn, B. N. Jensen, N. B. Krarup, and I. Wodstrup.⁹² These authors found that the addition of protamine to insulin leads to the formation of a salt (protamine-insulin) which is less soluble at about p_H 7 than is ordinary insulin; absorption of the injected material is therefore less rapid, and the complex continues to exercise a hypoglycaemic action for about 12 hours compared with 5–6 hours for ordinary insulin. Clinical tests showed that protamine-insulin gives very satisfactory results in the treatment of diabetes, particularly those cases where control of the blood-sugar with ordinary insulin is not too satisfactory. Various protamines have been used to form these complexes. H. C. Hagedorn and his colleagues used those derived from the sperm of the rainbow trout (*salmiridin*) and from mackerel (*scombrine*), but other basic proteins give similar results; amongst others, spermine⁹³ (prepared from the pancreas) and histones have been used.

A further step forward was made by D. A. Scott and A. M. Fisher. Following on their work on the rôle of zinc in the crystallisation of insulin, these authors found that the addition of a small amount of zinc (as zinc chloride, sulphate, etc.) led to a marked prolongation of the hypoglycaemic action of the hormone,⁹⁴ and they subsequently observed that zinc has a similar effect on protamine-insulin⁹⁵ (with amounts of zinc as small as 1 mg. Zn/500 units). The mixture called protamine zinc insulin is now used

⁹² *J. Amer. Med. Assoc.*, 1936, **106**, 177; H. C. Hagedorn, *Proc. Roy. Soc. Med.*, 1937, **30**, 11.

⁹³ A. M. Fisher and D. A. Scott, *J. Pharm. Exp. Ther.*, 1936, **58**, 93; 1937, **61**, 21.

⁹⁴ D. A. Scott and A. M. Fisher, *ibid.*, 1935, **55**, 206.

⁹⁵ *Idem*, *J. Biol. Chem.*, 1936, **114**, lxxxviii; *J. Pharm. Exp. Ther.*, 1936, **58**, 78; 1937, **61**, 21.

extensively for the treatment of diabetes, and most authorities on the subject agree that it has many advantages over ordinary insulin. Severe cases of this disease can usually be controlled by two injections of protamine zinc insulin per day,⁹⁶ and, if necessary, a little ordinary insulin can be added to the mixture to deal with the glucose absorbed shortly after a carbohydrate-containing meal. The value of the "new insulins" has been discussed by G. Graham,⁹⁷ who also gives an interesting account of the changes in the treatment of diabetes during the past fifteen years.

The addition of zinc stabilises in some way the suspension of protamine-insulin, but the delay in the response to insulin (or protamine-insulin) is not yet fully explained. Zinc, or some other metal, may be responsible for the combination of insulin and protamine,⁹⁵ and the presence of zinc in the pancreas and the ready crystallisation of the hormone when zinc is present⁹⁸ suggest that this metal may be a factor in the liberation and action of insulin in the body. Various other metals have been tested and some found to have an action similar to that of zinc.⁹⁹

During recent years renewed interest has been shown in the relationship between the anterior pituitary and carbohydrate metabolism. B. A. Houssay and A. Biassotti¹ found in 1931 that the removal of the pituitary gland greatly reduced the symptoms of diabetes produced by removal of the pancreas, and later experiments by Houssay and his colleagues² showed that intact animals

⁹⁶ For the earlier work on this subject, see H. C. Hagedorn *et al.*, ref. (92); O. Leyton, *Brit. Med. J.*, 1936, i, 443; R. D. Lawrence and N. Archer, *ibid.*, p. 487; H. F. Root, P. White, A. Marble, and E. H. Stotz, *J. Amer. Med. Assoc.*, 1936, **106**, 180; R. B. Kerr, C. H. Best, W. R. Campbell, and A. A. Fletcher, *Canadian Med. Assoc. J.*, 1936, **34**, 400. For more recent work, see H. C. Hagedorn (*Schweiz. med. Woch.*, 1938, **68**, 37) and G. Graham, ref. (97).

⁹⁷ *Lancet*, 1938, **235**, 1, 62, 121.

⁹⁸ D. A. Scott, *Biochem. J.*, 1934, **28**, 1592; D. A. Scott and A. M. Fisher, *ibid.*, 1935, **29**, 1048; *Trans. Roy. Soc. Canada*, 1938, **32**, 55. Analyses, by these authors, of crystalline zinc-insulin, cobalt-insulin, cadmium-insulin and nickel-insulin show that the metals concerned are chemically combined constituents of the compounds. The same authors (*J. Clin. Invest.*, 1938, **17**, 725) have also found that the zinc content of the pancreas of diabetics, at autopsy, is only one-half that normally present.

⁹⁹ For the literature, see E. M. Bavin and W. A. Broom (*Quart. J. Pharm.*, 1937, **10**, 327), who report that magnesium and iron behave like zinc in that small quantities prolong the hypoglycaemia, whereas large amounts completely inhibit the normal insulin response. These authors (W. A. Broom and E. M. Bavin, *ibid.*, p. 334) have also shown that the addition of zinc to tannic acid-insulin prolongs the hypoglycaemic effect of this complex.

¹ *Endocrinology*, 1931, **15**, 511.

² Summarised by B. A. Houssay, *New Engl. J. Med.*, 1936, **214**, 961, 971; cf. also H. M. Evans, K. Meyer, M. E. Simpson, and F. L. Reichert, *Proc. Soc. Exp. Biol. Med.*, 1932, **29**, 857.

could be rendered temporarily diabetic by the injection of extracts of the anterior pituitary. These observations have been confirmed by many investigators, and the suggestion naturally arose as to the possibility that diabetes in man might be due, in some cases, to hyperactivity of the anterior pituitary. Although no final answer can yet be made to this question, considerable progress has been recorded during the past three years as a result of the work of F. G. Young and several other authors. By prolonged injections of large amounts of crude saline extracts of fresh anterior pituitary glands, F. G. Young has succeeded in producing a permanent diabetic condition in normal dogs.³ These animals have lived for long periods (over one year) after the cessation of the injections, and have, during this period, shown hyperglycaemia, glycosuria and excretion of "acetone-bodies." The dogs retained full vigour, and no insulin treatment was found necessary; to abolish the glycosuria with a normal (high-protein) diet, these dogs required about 60 units of insulin per day. These crude ox anterior pituitary extracts have a diabetogenic action on dogs, sometimes on cats and rabbits, but not to any appreciable extent on mice, rats and guinea-pigs.⁴ More recent studies on the "diabetogenic factor" of the anterior pituitary have confirmed the view that this factor⁵ is probably complex; the glycotropic and thyrotropic factors of this gland are possibly constituents of this complex, but prolactin is not.⁶ Somewhat similar views as to the complexity of this principle have been put forward by C. N. H. Long,⁷ who considers that there are two components, one heat-labile and the other heat-stable. It would be unwise at present to speculate as to whether this complex is responsible, wholly or in part, for the occurrence of diabetes in man, but it is almost certain that our knowledge about this disease will be considerably enriched by these fundamental investigations. The observation that some of these dogs, rendered diabetic by pituitary extracts, have little or no islet tissue in the pancreas⁸ may help towards the solution of this problem.

Mention has been made above of the glycotropic factor of the

³ *Lancet*, 1937, **233**, 372. This observation has been confirmed by J. Campbell and C. H. Best (*Lancet*, 1938, **234**, 1444).

⁴ F. G. Young, *Biochem. J.*, 1938, **32**, 513.

⁵ The term "diabetogenic hormone" adopted by some authors is apt to be misleading, and its use should not be encouraged [see F. G. Young, ref. (4)]. Recent work on the various hormones of the anterior pituitary has been well summarised by J. B. Collip (*Edin. Med. J.*, 1938, **45**, 782).

⁶ F. G. Young, *Biochem. J.*, 1938, **32**, 524.

⁷ *Medicine*, Baltimore, 1937, **16**, 215.

⁸ K. C. Richardson and F. G. Young, *Lancet*, 1938, **234**, 1098.

anterior pituitary, a factor which may be a component of the more complex diabetogenic factor. The work of O. Cope and H. P. Marks⁹ showed that the injection of extracts of this gland into normal rabbits neutralised the effect of insulin subsequently injected, and more recent work by F. G. Young has thrown considerable light on the nature and properties of the active agent. This "anti-insulin" or "glycotropic"¹⁰ factor does not significantly alter the blood-sugar of fasting rabbits, nor does the injection of large amounts cause glycosuria or ketonuria in dogs (*i.e.*, the substance is not diabetogenic by itself), but it produces a complete insensitivity to the hypoglycaemic action of insulin. It is not identical with prolactin,¹¹ or with the thyrotropic and gonadotropic hormones or the oxytocic or vasopressor substances of the pituitary.¹² The mechanism of the anti-insulin effect of the glycotropic substance has been studied by several investigators¹³ and it is fairly generally agreed that the hyperglycaemic action of adrenaline is not essentially concerned with this response; the glycotropic substance appears rather to act by antagonising the action of insulin both in the liver and in the peripheral tissues.¹²

Isotopes in the Study of Metabolism.

It was perhaps only to be expected that biochemists would explore the possibility of using heavy hydrogen as a new weapon for attacks on many of the unsolved problems of metabolism. Previous to the discovery of this isotope, G. von Hevesy¹⁴ had studied the fate of lead containing one of its radioactive isotopes (Ra-D), but this method of labelling an element has very limited possibilities. A much wider field was opened by the discovery of deuterium and later heavy nitrogen (N¹⁵), accompanied by the elaboration of sensitive methods for the detection and determination of very small amounts of the heavy isotopes.

The first workers to use deuterium for the study of intermediate metabolism were R. Schoenheimer and D. Rittenberg, who introduced the label or "tag" by catalytic reduction of unsaturated

⁹ *J. Physiol.*, 1934, **83**, 157.

¹⁰ The expression "glycotropic" was first suggested by F. G. Young (*Lancet*, 1936, **231**, 297).

¹¹ F. G. Young, *Chem. and Ind.*, 1937, **56**, 292; *Biochem. J.*, 1938, **32**, 524; *Chem. and Ind.*, 1938, **57**, 1190.

¹² *Idem*, *Biochem. J.*, 1938, **32**, 1521.

¹³ H. P. Himsworth and D. B. M. Scott, *J. Physiol.*, 1938, **91**, 447; **92**, 183; F. G. Young, *ref.* (12); H. P. Marks and F. G. Young, *J. Physiol.*, 1938, **93**, 61.

¹⁴ *Biochem. Z.*, 1926, **173**, 175.

fats in the presence of deuterium.¹⁵ The saturated fats obtained, and in later experiments sterols, bile acids, etc., cannot be distinguished from the natural analogues by ordinary chemical methods. In this way deuterium is attached to carbon with the production of compounds which are so little different from the "normal" compounds that one is probably justified in believing that the animal body will treat the labelled and the natural products in exactly the same way. The body has extraordinary powers for distinguishing between certain optical isomers, and there are numerous observations which show that a very slight change in one group of a very large molecule may have a profound effect on the physiological or pharmacological action of a compound, but as yet there is no evidence that the metabolism of stearic acid containing two atoms of deuterium per molecule differs from that of the natural acid. Furthermore there is good reason to believe that the removal of deuterium from, and its introduction into, fatty acids and other compounds are not due to a mere physical exchange of hydrogen and deuterium (R. Schoenheimer and D. Rittenberg¹⁶). Normal constituents of our food can thus be administered to animals in such a form that many molecules have labels attached to them, and perhaps even more important, methods are available for the detection of the label in various fractions of the animal body. The sensitivity of these methods is such that some of the labelled products can be readily detected when diluted with more than 1,000 times their weight of natural product.

An excellent review of the use of isotopes in the study of intermediate metabolism is given by R. Schoenheimer and D. Rittenberg,¹⁶ who discuss the position up to the end of 1937. Since this field has not been covered in these Reports, a brief account of some of the main results might be welcomed. The feeding of deuterio-fats leads to the deposition of a large part of the fat in the fat depots, with smaller amounts in the liver, etc.¹⁷ B. Cavanagh and H. S. Raper¹⁸ in similar studies showed that the absorption of deuterium-containing fat is almost complete, and that considerable amounts

¹⁵ *J. Biol. Chem.*, 1935, **111**, 163; D. Rittenberg and R. Schoenheimer, *ibid.*, p. 169; R. Schoenheimer, D. Rittenberg, and M. Graff, *ibid.*, p. 183; R. Schoenheimer and D. Rittenberg, *ibid.*, 1936, **113**, 505; **114**, 381; R. Schoenheimer, D. Rittenberg, B. N. Berg, and L. Rousselot, *ibid.*, 1936, **115**, 635. W. E. van Heyningen, D. Rittenberg, and R. Schoenheimer (*ibid.*, 1938, **125**, 495) have recently described two methods for the preparation of fatty acids containing deuterium. In one method the exchange occurs at the α -carbon atom only.

¹⁶ *Science*, 1938, **87**, 221; cf. also review by A. Krogh, *Enzymologia*, 1938, **5**, 185.

¹⁷ R. Schoenheimer and D. Rittenberg, *J. Biol. Chem.*, 1935, **111**, 175.

¹⁸ *Nature*, 1936, **137**, 233.

of the fatty acids containing deuterium enter into the lipines of organs such as the liver and kidney; this observation offers strong support for the view that the lipines are actively concerned in the metabolism of fat.

Investigations dealing with the theory of fatty acid desaturation have yielded interesting and fundamental results. This theory, that fatty acids can be desaturated in the liver and possibly other organs, was previously supported by evidence which was not entirely convincing, but the work of R. Schoenheimer and D. Rittenberg now appears to show quite definitely that this change does occur. Deutero-unsaturated acids were isolated from mice which had received deutero-stearic acid,¹⁹ and evidence of the reverse change, *i.e.*, the saturation of unsaturated fatty acids, has also been obtained.²⁰ Desaturation does not appear to be effected during the absorption of fatty acids by the intestinal wall,²¹ and so far these experiments have not established the site of this process; in all probability the responsibility will largely fall on that hard-worked organ, the liver. In further experiments with deutero-fats R. Schoenheimer and D. Rittenberg have confirmed the view that stearic acid can be converted into palmitic acid,²² and they have shown also that administered deutero-butyric and -hexoic acids are not used for the synthesis of higher fatty acids for fat-storage, but are rapidly and completely oxidised in the body.²³ In these investigations it is improbable that the changes observed are due to simple exchange of hydrogen between the substances concerned and the water in which they are dissolved, since deuterium-free fatty acid²⁴ and cholesterol²⁵ were isolated from chicks which had developed in heavy water-enriched eggs, and deuterium-free lysine from mice whose body fluids had contained heavy water for more than three months.²⁶ The claim that proteolytic enzymes may introduce carbon-bound deuterium into amino-acids from heavy water²⁷ is not confirmed by G. L. Foster, A. S. Keston, D. Rittenberg, and R. Schoenheimer.²⁸

H. M. Barrett, C. H. Best, and J. H. Ridout²⁹ have recently made

¹⁹ R. Schoenheimer and D. Rittenberg, *J. Biol. Chem.*, 1936, **113**, 505.

²⁰ D. Rittenberg and R. Schoenheimer, *ibid.*, 1937, **117**, 485.

²¹ Cf. R. Schoenheimer and D. Rittenberg, *Science*, 1938, **87**, 221.

²² R. Schoenheimer and D. Rittenberg, *J. Biol. Chem.*, 1937, **120**, 155.

²³ D. Rittenberg, R. Schoenheimer, and E. A. Evans, *ibid.*, p. 503.

²⁴ R. Schoenheimer and D. Rittenberg, *ibid.*, 1936, **114**, 381.

²⁵ D. Rittenberg and R. Schoenheimer, *ibid.*, 1937, **121**, 235.

²⁶ Cf. ref. (21).

²⁷ J. A. Stokol and W. H. Hamill, *J. Biol. Chem.*, 1937, **120**, 531.

²⁸ *Ibid.*, 1938, **124**, 159.

²⁹ *J. Physiol.*, 1938, **93**, 367; cf. also H. M. Barrett, C. H. Best, and J. H. Ridout, *J. Biol. Chem.*, 1938, **123**, iii.

use of deuterium as an indicator for the study of the source of the fat which accumulates in the liver when animals are maintained on a diet poor in lipotropic factors or when certain extracts of the anterior pituitary gland are administered.³⁰ Using a specially devised rapid and relatively simple micro-density method for the determination of deuterium oxide, these authors have confirmed the view that the fat depots supply most if not all of the fat which accumulates in the liver during fasting, or after administration of anterior pituitary extracts, or when mice are exposed to carbon tetrachloride vapour. When animals containing deutero-fat in the fat reserves are fed on a diet which is low in protein and other lipotropic factors but rich in carbohydrate, they accumulate liver-fat which does not come from the depots but most probably from the food carbohydrate. These authors have also obtained evidence of the *in vitro* and *in vivo* stability of the label of deutero-fats.

The metabolism of proteins and amino-acids is now being investigated by similar methods. R. Schoenheimer, D. Rittenberg, M. Fox, A. S. Keston, and S. Ratner³¹ have introduced heavy nitrogen into glycine and hippuric acid, and have shown that the latter can be absorbed from the intestinal tract without being hydrolysed; the results suggest also that glycine may be used directly for hippuric acid formation. A. Krogh and H. H. Ussing³² have used a rather different method for the study of protein metabolism. The maintenance of a fairly constant concentration of heavy water in an animal results in the introduction of deuterium into amino-acids, attached in part to the asymmetric carbon atoms in the growing foetus but to other carbon atoms in the mature organism. The proteins of the viscera of these animals showed this exchange of hydrogen to a greater extent than did the proteins of muscle and skin, owing presumably to the less reactive elastin, collagen and keratin.³³ The lipide of the rat showed no similar exchange of hydrogen and deuterium.

Radioactive elements have been used by many authors for

³⁰ For a review of this work on lipotropic factors, etc., see D. L. Maclean, J. H. Ridout, and C. H. Best, *Brit. J. Exp. Path.*, 1937, **18**, 345; C. H. Best and J. H. Ridout, *Amer. J. Physiol.*, 1938, **122**, 67; C. H. Best and J. Campbell, *J. Physiol.*, 1938, **92**, 91; H. J. Channon, G. N. Jenkins, and J. A. B. Smith, *Biochem. J.*, 1937, **31**, 41; H. J. Channon, J. V. Loach, and G. R. Tristram, *ibid.*, 1938, **32**, 1332.

³¹ *J. Amer. Chem. Soc.*, 1937, **59**, 1768; cf. also H. H. Ussing (*Nature*, 1938, **142**, 399), who has used deutero-amino-acids for the study of protein metabolism.

³² *Compt. rend. Trav. Lab. Carlsberg*, 1938, **22**, 282; cf. also J. A. Stekol and W. H. Hamill, *Proc. Soc. Exp. Biol. Med.*, 1937, **35**, 591, and G. L. Foster, D. Rittenberg, and R. Schoenheimer, *J. Biol. Chem.*, 1938, **125**, 13.

³³ H. H. Ussing, *Skand. Arch. Physiol.*, 1938, **78**, 225.

the study of biological problems. The use of natural radio-elements is obviously rather limited, but a much wider application is possible with artificially produced radio-elements (*e.g.*, the isotopes of carbon, phosphorus, sodium and calcium).³⁴ Labelled (radioactive) phosphorus, prepared from sulphur by neutron bombardment, was injected subcutaneously, as sodium phosphate, into a rabbit by L. A. Hahn, G. C. Hevesy, and E. C. Lundsgaard.³⁵ Within 27 days, 45% of this phosphorus was excreted in the urine and 11% in the faeces, and the average time a phosphorus atom remains in the body was found to be 30 days. An exchange of phosphorus atoms by bone still continues after the lapse of 21 days. A similar exchange occurs in teeth, and the replacement of 1% of the phosphorus of a human tooth by phosphorus derived from the food takes about 250 days.³⁶ Ingestion of radioactive phosphorus (as Na_2HPO_4) by fasting rats is followed by the appearance of this isotope in the phospholipins of all the tissues examined, and the results suggest that the liver and intestine and possibly the kidney participate in phospholipin synthesis.³⁷ A considerable amount of this radioactive phosphorus is used for lipin formation within 30 minutes of the injection of the phosphate.³⁸ Similar conclusions are reached by W. E. Cohn and D. M. Greenberg, who state that brain has a slow turnover of phosphorus, but other tissues show a rapid uptake in the first 10 hours.³⁹

Other isotopes have not escaped attention, and amongst those which have given promising results are the radioactive isotopes of sodium,⁴⁰ potassium,⁴¹ sulphur,⁴² iodine and iron. The value of what has been described as "this scientific game of tag" need not be emphasised, and it seems almost certain that the use of labelled

³⁴ Cf. G. von Hevesy and F. A. Paneth, *Science Progress*, 1937, **32**, 38.

³⁵ *Biochem. J.*, 1937, **31**, 1705.

³⁶ G. Hevesy, J. J. Holst, and A. Krogh, *Kgl. Danske Videnskab. Selskab*, 1937, **13**, 34.

³⁷ I. Perlman, S. Ruben, and I. L. Chaikoff, *J. Biol. Chem.*, 1937-8, **122**, 169; B. A. Fries, S. Ruben, I. Perlman, and I. L. Chaikoff, *ibid.*, 1938, **123**, 587.

³⁸ M. J. L. Dols, B. C. P. Jansen, G. J. Sizoo, and F. Barendregt, *Nature*, 1938, **141**, 77.

³⁹ *J. Biol. Chem.*, 1938, **123**, 185; cf. also S. F. Cook, K. G. Scott, and P. Abelson (*Proc. Nat. Acad. Sci.*, 1937, **23**, 528), who had previously shown that radio-phosphorus is deposited in all the tissues of growing chicks examined but principally in bone and muscle.

⁴⁰ J. G. Hamilton and R. S. Stone, *Proc. Soc. Exp. Biol. Med.*, 1937, **35**, 595; J. G. Hamilton, *Proc. Nat. Acad. Sci.*, 1937, **23**, 521.

⁴¹ D. M. Greenberg, M. Joseph, W. E. Cohn, and E. V. Tufts, *Science*, 1938, **87**, 438.

⁴² H. Borsook, G. Keighley, D. M. Jost, and E. McMillan, *ibid.*, 1937, **86**, 525.

elements will undoubtedly throw much light on many of the mysteries of fat and possibly protein metabolism. Other aspects of biochemistry in which one may confidently anticipate useful progress as a result of the use of these isotopes are those concerned with some of the hormones, enzyme action, the chemistry of immunity, and the action of certain drugs.

Chemotherapy.

Sulphanilamide and Related Drugs.—The claim⁴³ that the discovery of sulphanilamide, prontosil, and related compounds was probably the most important advance in chemotherapy for many years has been fully substantiated and amazing progress has been made in this branch of "chemical warfare" during the past year. The main efforts have been devoted to a search for new sulphonamide derivatives more powerful and possibly less toxic than sulphanilamide, and to investigations on the mode of action of these drugs. Under the first heading might be included the preparation of new derivatives for the treatment of bacterial infections which resist the action of prontosil and sulphanilamide, and in this field the discovery of M. & B. 693, mentioned below, is of outstanding importance.

The literature on sulphanilamide (IV) and its congeners is now so colossal that it is not possible to mention more than a few of the published papers. Excellent comprehensive reviews of the discovery of the drugs of this group and the work done in this field are given by L. P. Garrod,⁴⁴ P. H. Long and E. A. Bliss,⁴⁵ C. Levaditi,⁴⁶ and L. E. H. Whitby.⁴⁷ The value of these drugs for the treatment of the majority of hæmolytic streptococcal infections is, to quote the words of L. P. Garrod, "now a matter of almost universal experience and not one demanding proof." Amongst other diseases in which successful results are frequently obtained with sulphanilamide administration are certain staphylococcal, pneumococcal, meningococcal and gonococcal infections, gas gangrene, typhoid fever, undulant fever, and certain skin infections. There is not, however, unanimous agreement as to the efficacy of sulphanilamide treatment in all these infections. It is generally agreed that there are many infections (*e.g.*, tuberculosis,⁴⁸ syphilis, rheumatic fever,

⁴³ *Ann. Reports*, 1937, **34**, 398.

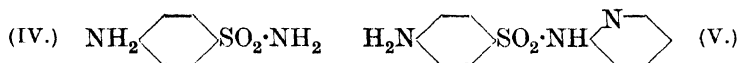
⁴⁴ *Lancet*, 1938, **234**, 1125, 1178.

⁴⁵ *Ann. Intern. Med.*, 1937, **11**, 575.

⁴⁶ *Schweiz. Z. allg. Path. Bakt.*, 1938, **1**, 365. ⁴⁷ *Lancet*, 1938, **235**, 1095.

⁴⁸ A. R. Rich and R. H. Follis (*Bull. Johns Hopkins Hosp.*, 1938, **62**, 77) found, however, that sulphanilamide has a distinct inhibitory effect on the development of tuberculous lesions in guinea-pigs infected with a human strain. Less striking results were obtained by G. A. H. Buttle and H. J. Parish (*Brit. Med. J.*, 1938, *ii*, 776).

and leprosy) where this drug has no curative or preventive action. The treatment of virus diseases (*e.g.*, infantile paralysis, influenza, and encephalitis) with sulphanilamide is usually ineffective.⁴⁹



The discovery of prontosil and the later observation that the less complex sulphanilamide has a similar therapeutic value have been followed by numerous attempts to obtain compounds with a higher efficiency, a lower toxicity or a wider range of action on bacteria. Thousands of these derivatives have been prepared and tested by *in vitro* experiments; several have given sufficiently promising results to warrant trial on man. The information obtained, even where the results were of a negative character, will certainly be of considerable value when sufficient evidence is available to correlate the *in vitro* and *in vivo* effects with the chemical constitutions of these compounds. It has already been established that the sulphonamide group is not the only one effective in this class, for certain sulphones have an activity equal to that of sulphanilamide.⁵⁰ Substitution in the amino-group or replacement of one hydrogen of the sulphonamido-group does not necessarily produce inactive products, but few other generalisations can be made at present. The testing of these compounds is largely a matter of "tedious empirical trial and error" (L. E. H. Whitby⁴⁷).

The most promising of the new derivatives is undoubtedly 2-(*p*-aminobenzenesulphonamido)pyridine (M. & B. 693 or T. 693) (V). L. E. H. Whitby⁵¹ has shown that this substance is chemotherapeutically active, in experimental infections in mice, against pneumococci of Types I, II, III, V, VII, and VIII. Sulphanilamide has relatively little action on these organisms, and since M. & B. 693 is at least as lethal to certain other organisms (haemolytic streptococci, meningococci, etc.) as is sulphanilamide and its toxicity is apparently less than that of the last-named,⁵²

⁴⁹ F. O. MacCallum and G. M. Findlay (*Lancet*, 1938, **235**, 136) found, however, that sulphanilamide and a glucose derivative of 4:4'-diaminodiphenylsulphone protect a large percentage of mice against the virus of *lymphogranuloma inguinale* introduced intracerebrally. C. Levaditi (*Compt. rend. Soc. Biol.*, 1938, **127**, 958; **128**, 138) also found certain sulphonamides effective in the treatment of virus infections in small animals.

⁵⁰ Cf. *Ann. Reports*, 1937, **34**, 421.

⁵¹ *Lancet*, 1938, **234**, 1210.

⁵² R. Wien, *Quart. J. Pharm.*, 1938, **11**, 217. Cf., however, E. K. Marshall, A. C. Bratton, and J. T. Litchfield (*Science*, 1938, **88**, 597), who have reached the opposite conclusion and advise caution in the use of 2-sulphanilamidopyridine.

it is receiving extensive clinical trials. Almost invariably satisfactory results have so far been reported. A marked reduction in the mortality rate amongst patients with lobar- and bronchopneumonia has been observed⁵³ and successful results have been obtained in cases of gonorrhoea⁵⁴ and pneumococcal meningitis.⁵⁵

The mode of action of these drugs has been the subject of many investigations.⁵⁶ The theory most commonly accepted in this country is that they exert a bacteriostatic action, thus preventing the rapid development of the organisms; the body is then able to overcome the infection by its normal defence mechanisms, *e.g.*, by phagocytosis by the leucocytes. Sulphanilamide has some action on the capsules of streptococci⁵⁷ and M. & B. 693 has a similar action on the pneumococcus capsule,⁵⁸ and this direct action may play a part in the inactivation of the organisms. The work of J. S. Lockwood⁵⁹ suggests that sulphanilamide exerts its action by preventing streptococci from utilising serum proteins for growth purposes, possibly by the inactivation of an enzyme. Other investigators have suggested that these drugs neutralise toxins produced by bacteria or that they stimulate phagocytic activity or other defence mechanisms, but the evidence in favour of these hypotheses does not appear to be conclusive.

The marked specificity of many of these drugs is another interesting feature. The selective action on certain bacteria

⁵³ M. Telling and W. A. Oliver, *Lancet*, 1938, **234**, 1391; G. M. Evans and W. F. Gaisford, *ibid.*, **235**, 14; J. M. Christie, *ibid.*, p. 281; S. C. Dyke and G. C. K. Reid, *ibid.*, p. 1157.

⁵⁴ V. E. Lloyd, D. Erskine, and A. G. Johnson, *Lancet*, 1938, **234**, 1305; T. Anwyl-Davies, *Practitioner*, 1938, **141**, 496; F. J. T. Bowie, *Brit. Med. J.*, 1938, ii, 283. R. C. L. Batchelor, R. Lees, M. Murrell, and G. I. H. Braine (*Brit. Med. J.*, 1938, ii, 1142) have recently reported on the treatment of 102 cases of gonococcal infection with M. & B. 693, and conclude that this drug is the most potent anti-gonococcal agent available at present.

⁵⁵ For the literature, see ref. (47).

⁵⁶ Cf. reviews, refs. (44) and (47). A. Fleming (*Lancet*, 1938, **235**, 74, 564) has carried out a full investigation of the antibacterial power of M. & B. 693 against haemolytic streptococci and pneumococci, and has shown that the increased antibacterial power of the blood of patients taking this drug lies in the serum. This drug does not, however, prevent capsulation of pneumococci. E. A. Bliss and P. H. Long (*J. Amer. Med. Assoc.*, 1937, **109**, 1524) conclude that sulphanilamide controls streptococcal and certain other infections in mice largely by a bacteriostatic action. In the control of infections of the urinary tract, a bactericidal action is also exerted (P. H. Long and E. A. Bliss, *South. Med. J., Alabama*, 1938, **31**, 308).

⁵⁷ C. Levaditi and A. Vaisman, *Compt. rend. Soc. Biol.*, 1935, **119**, 946; **120**, 1077.

⁵⁸ L. E. H. Whitby, *Lancet*, 1938, **234**, 1210; M. Telling and W. A. Oliver, *ibid.*, p. 1391.

⁵⁹ *J. Immunol.*, 1938, **35**, 155.

suggests a specific combination with "receptor" groups in the organism, and this phenomenon might prove of value in bacteriological and immunological investigations. Whether the prolonged administration of these drugs will lead to the development of drug-resistant strains of the organisms has not been established, but it is perhaps fortunate that there is now available a large number of widely differing drugs of this type for the eradication of these undesirable strains.

The outstanding success of this work on sulphanilamide, etc., has naturally led to their fairly widespread use for almost any ailment from the common cold to rheumatism. Routine administration of the compounds for all types of infection is strongly deprecated by most authorities in this field, and it should be remembered that practically all these sulphonamides frequently produce some or all of the toxic effects referred to last year.⁶⁰ These symptoms, occurring often in 50% of the treated cases, are usually of a mild character, and can be controlled, but some fatalities have been recorded. The exact significance of the increased amount of porphyrin excreted in the urine following the administration of sulphanilamide to hospital patients⁶¹ has not been established, but it may be connected with hypersensitiveness to the drug, as shown by dermatitis in some cases.

E. K. Marshall and his colleagues have made important contributions on the absorption and excretion of sulphanilamide and many of its derivatives. Using a colorimetric method for the determination of these substances,⁶² they have continued their studies on the behaviour of the drugs in various animals.⁶³ They have observed that sulphanilamide given orally in solution is absorbed much more rapidly than when given in solid form, and that excretion of the drug in the urine is more rapid in the mouse than in the rat, dog or man.

Some Chemical Aspects of Immunity.

It is impossible to do justice to this important and rapidly developing subject in the space remaining for animal biochemistry.

⁶⁰ *Ann. Reports*, 1938, **34**, 423. A more complete account of the toxicity of sulphanilamide and the effects of large doses administered to various animals is given by E. K. Marshall, W. C. Cutting, and K. Emerson (*J. Amer. Med. Assoc.*, 1938, **110**, 252. Cf. also P. H. Long, *Ohio State Med. J.*, 1938, **34**, 977).

⁶¹ C. Rimington and A. W. Hemmings, *Lancet*, 1938, **234**, 770.

⁶² E. K. Marshall, *J. Biol. Chem.*, 1937, **122**, 263; E. K. Marshall and J. T. Litchfield, *Science*, 1938, **88**, 2273.

⁶³ E. K. Marshall, W. C. Cutting, and W. L. Cover, *Bull. Johns Hopkins Hosp.*, 1938, **63**, 318; E. K. Marshall and W. C. Cutting, *ibid.*, p. 328.

All that can be attempted is to indicate one or two of the advances which have been made in recent times and to show how immunochemical methods are being used to help to solve some of the problems of biochemistry. Excellent reviews⁶⁴ are available for those who wish to have a full account of this subject.

The chemical basis of the specificity of antigens has been extensively studied by the use of conjugated antigens, in which certain known groups have been attached to antigenic proteins (*e.g.*, serum globulin). For the preparation of these conjugated antigens K. Landsteiner and H. Lampl in 1917 first made use of the property of proteins of coupling, by virtue of the phenolic and iminazole groups which they contain, with diazonium compounds in alkaline solution, and during the past twenty years this method has been used, with very successful results, by numerous workers. Other reactions have been described for the introduction of new groups into proteins, but these have usually been of limited application. In a recent general method devised by R. F. Clutton, C. R. Harington, and T. H. Mead,⁶⁵ a compound containing a carboxyl group is converted into the acid azide, which is coupled, under mild conditions, with a protein. Using this technique, R. F. Clutton, C. R. Harington, and M. E. Yuill⁶⁶ have shown that both insulin and gelatin become antigenic when coupled with glucosidotyrosine; the antibodies produced by these complexes will react with glucosidotyrosyl-globulin, but for some unknown reason, not with the antigen used for the immunisation. In a further study the same authors⁶⁷ have prepared thyroxyl derivatives of serum globulin and albumin, and of thyroglobulin, and have found that immunisation with these complexes produces antisera which when injected into rats will protect against the normal physiological effects of exogenously administered thyroglobulin or thyroxine. The possible extension of this work to antisera against artificial compounds of proteins with other physiologically active compounds will be awaited with considerable interest.

There is much evidence, chemical as well as immunological, that a large variety of compounds are capable of reacting with proteins to form complexes quite different in immunological

⁶⁴ "The Specificity of Serological Reactions," by K. Landsteiner (Charles C. Thomas, Baltimore, 1936); "The Chemistry of Antigens and Antibodies," by J. R. Marrack (H. M. Stationery Office, London, 1938). Shorter reviews are given, in the *Ann. Rev. Biochem.*, by M. Heidelberger (1933, **2**, 503; 1935, **4**, 569) and by K. Landsteiner and M. W. Chase (1937, **6**, 621).

⁶⁵ *Biochem. J.*, 1937, **31**, 764.

⁶⁶ *Ibid.*, 1938, **32**, 1111.

⁶⁷ *Ibid.*, p. 1119.

properties from the original protein. Several types of hypersensitivity in man can undoubtedly be explained on the basis that the active agent combines with the body proteins to produce a complex which is "foreign" and antigenic to the body. Strong evidence in support of this view has been obtained by K. Landsteiner and M. W. Chase,⁶⁸ who have shown that true anaphylactic sensitisation can be effected in guinea-pigs by the cutaneous application of simple chemical substances, including 2:4-dinitrochlorobenzene, a typical incitant of contact dermatitis in man. Although the formation of antigenic conjugates will not account for all types of allergic response, these and similar immuno-chemical studies should throw much light on many aspects of allergy, including hypersensitivity to certain drugs, to hormones such as insulin, and to chemical substances which frequently produce dermatitis in industrial workers.

Other investigations to which reference should be made are those dealing with the mechanism of the antigen-antibody reaction, in particular the quantitative theory of the precipitin reaction propounded by M. Heidelberger.⁶⁹ Other workers⁷⁰ have isolated, from bacteria, antigens which when injected produce an active immunity similar to that produced by the whole bacterial cells, and in certain instances the non-protein nature of the bacterial antigens is strongly suggested; in one case at least the complex consists mainly, if not entirely, of polysaccharide linked to a phosphatide. Another interesting problem is that of the anti-hormones, the study of which was stimulated by the discoveries of J. B. Collip and his colleagues,⁷¹ but lack of space prevents a discussion of this and many other fascinating aspects of immunity. Sufficient has perhaps been said to indicate the progress which has been made and the bright prospects for the future. The rabbit has already worked wonders as a relatively inexpensive chemical assistant, and the delicate and highly specific immunological tests are certain to be of considerable use in the future study of the normal as well as the pathological animal.

A. WORMALL.

⁶⁸ *J. Exp. Med.*, 1937, **66**, 337, and earlier papers.

⁶⁹ See H. E. Stokinger and M. Heidelberger (*ibid.*, p. 251) and M. Heidelberger (*J. Amer. Chem. Soc.*, 1938, **60**, 242) for the literature.

⁷⁰ For the literature, see W. W. C. Topley, H. Raistrick, J. Wilson, M. Stacey, S. W. Challinor, and R. O. J. Clark, *Lancet*, 1937, **232**, 252; W. T. J. Morgan, *Biochem. J.*, 1937, **31**, 2003.

⁷¹ A discussion of the early work in this field is given by G. F. Marrian and G. C. Butler (*Ann. Rev. Biochem.*, 1937, **6**, 303; cf. also O. Wintersteiner and P. E. Smith, *ibid.*, 1938, **7**, 253).

PLANT BIOCHEMISTRY.

Introductory.

Any attempt to summarise the progress in any branch of chemistry for one year involves drastic selection, and the choice of some hundred odd references from the many hundreds available is always invidious. In the first part of this year's Report on Plant Biochemistry an attempt has been made to indicate some of the substances—carbohydrates, enzymes, pigments, etc.—in which the plant chemist is interested. The plant chemist, as distinct from the structural organic chemist, may still be said to blaze the trail for his colleague, although the distance between them is ever decreasing. The problem of starch is still engaging the attention of chemists the world over, and a reconciliation between results and theories based solely on chemical grounds and those derived from a study of enzymic reactions appears to be very much nearer than was formerly the case.

The survey of the anthocyanins commenced in 1931 continues, and of particular interest in this field is the discovery of new types based on hydroxy-cyanidins and -pelargonidins. Nitrogenous anthocyanins also are reported.

For reasons of space, only a brief review of some chemical aspects of micro-organisms has been possible, and a summary of important work on the substances necessary for the growth of higher and lower plants is held over until next year.

Some Plant Products.

Starch and Amylases.—It is proposed in succeeding paragraphs to discuss starch mainly with reference to amylase action, but a preliminary reference to the more chemical aspects may be made. Views on the constitution of starch have by no means reached finality, but it may be said that two theories stand out beyond others. On the one hand there is the well-established calculation of Haworth and his school, based on the end-group assay method, which indicates a chain length for the starch molecule corresponding to 25—30 glucose units combined through α -glycosidic links. These primary units are associated into physical aggregates of much larger dimensions. On the other hand Staudinger has long held the view that macro-molecules as distinct from molecular aggregates exist in starch, a view based largely on physical considerations. In recent experiments described by H. Staudinger and E. Husemann^{1,2} it was shown that after acetylation of potato, and later of wheat starch, a regenerated starch was obtained in which the degree of

¹ *Annalen*, 1937, **527**, 195.

² *Ber.*, 1938, **71**, 1057.

polymerisation was practically unchanged. Phosphorus-free starch was used, which by osmotic pressure measurements had a molecular weight of 286,000, corresponding to a polymerisation degree of 1770. By rapid hydrolysis with *N*-hydrochloric acid another preparation was obtained with a polymerisation degree of only 600. The regenerated compounds after acetolysis possessed polymerisation degrees of 1640 and 530 respectively. It is suggested that the macro-molecules are extremely sensitive to chemical disruption and the presence of only a trace of atmospheric oxygen in the solvent exerts an enormous effect on the degree of polymerisation. This probably explains why such results have not hitherto been obtained, and the slight lowering in degree of polymerisation observed is of no significance in view of the great difficulty of avoiding disturbing influences. The results were confirmed by viscosity measurements.

It is suggested that the starch macro-molecules must be quite different from the cellulose micelles. The structure of starch is envisaged as consisting of short branched coils, the glucose chains being linked from chain to chain through the aldehyde and hydroxyl groups. Such a conception fulfils physical requirements and also accounts for the occurrence of tetramethyl glucose in the proportions obtained by methylation methods, and for the lack of aldehydic properties in starch itself.

The activity of preparations of amylases has been investigated by J. Blom, A. Bak, and B. Braae,³ who find that the effects of heating, acidifying or adsorbing on starch are reflected in the subsequent action of the enzymes. Thus there are changes in the power to liquefy and saccharify starch, and the action on the starch-iodine property is modified. A study of the changes effected by pretreatment of the amylase preparation is of use in revealing the presence of one or the other of the only two forms discovered, namely, the liquefying α -amylase and the saccharogenic β -amylase. The authors confirm that the usual preparations of malt amylase are mixtures of the two types and find similar mixtures in preparations from *Aspergillus oryzae*; one form only was present in the case of bacterial and pancreatic amylases.

In a further contribution⁴ on the decomposition of starch by amylases these authors employ a commercial preparation, superclastase, shown to contain only α -amylase. The starch is decomposed only to the extent of 40%, after which the action of the amylase ceases or becomes exceedingly slow. Dextrins are first formed and in the later stages of the action the enzyme is catalysing the breakdown to maltose of such dextrins. The products of the

³ *Z. physiol. Chem.*, 1937, **250**, 104.

⁴ *Ibid.*, 1938, **252**, 251.

action were studied, not by the more usual method of fractional precipitation with alcohol, but after fermentation of the maltose with brewer's or baker's yeast.

The progressive changes in iodine coloration effected during hydrolysis of starch by the two amylases, indicated in a previous reference,³ have been studied quantitatively by C. S. Hanes and M. Cattle,⁵ who have examined the absorption characteristics of the compounds produced during the action. They find that the two amylases are directly distinguishable from very early stages of the respective reactions by the manner in which the absorption characteristics change. Moreover, it is claimed that by plotting colour, or absorption, and reducing power relationships, it is possible to correlate changes in iodine coloration and the liberation of reducing groups as hydrolysis proceeds. These considerations may be said to have two important bearings on studies on starch and its enzymic breakdown: firstly, these methods provide a basis of additional refinement in the investigation of amylase action; secondly, they have a direct bearing on theories of the constitution of starch. It is considered that "colouring groups" are evenly distributed along the molecular chain structure of starch such that the molecule may be divided into a number of portions which contain equivalent numbers of "colouring groups." The difference in iodine colour observed in different degradation products is related to a molecular association. The action of α -amylase involves a marked alteration in iodine colour and this is thought to be due to a preliminary disruption of molecular associations, followed by destruction of "colouring groups," achroic dextrans being finally formed. With β -amylase, however, there is progressive reduction in "colouring groups," whilst maltose fragments are broken off at the end of the chain. The failure to break down the molecular associations of the residual dextrans is reflected in the relative constancy of the absorption characteristics of the iodine compounds formed.

It is a well known fact that the action of amylases on starch results in the production amongst other products of the so-called stable or limit dextrans. At the same time, none of the structures so far suggested, largely on chemical grounds, for the starch molecule satisfactorily explains the inability of the usual enzymes to degrade the dextrin further, or shows exactly why the hydrolytic action ceases at a certain point. Amongst many investigations on this subject may be mentioned those of K. Myrbäck, B. Örtenblad and K. Ahlborg,^{6, 7} who suggest that the formation of such dextrans is

⁵ *Proc. Roy. Soc., B*, **125**, 387.

⁶ *Compt. rend. Trav. Lab. Carlsberg, Ser. chim.*, **1938**, **22**, 357.

⁷ *Biochem. Z.*, **1938**, **297**, 160, 172, 179.

due to the non-uniform character of the starch molecule; whilst accepting the Haworth conception of chains of maltose as the basis of the starch molecule, they consider that there may also be branched chains or abnormal types of linkage, and that the proportion of the molecule represented by such an arrangement would be resistant to enzyme action. They have obtained the limit dextrin (or α -amylo-dextrin) by the action of β -amylase on starch, and by alcohol precipitation have obtained a number of fractions which appear to have widely differing molecular weights and phosphorus contents. The latter varied from 0.3% to 0.8% and the authors consider that the whole of the phosphorus of the original starch remains in the limit dextrin, provided that phosphatase is absent. The suggestion is made that the presence of a phosphoric acid group in the molecule, or at certain points in the chain, protects the associated residues from amylase action. The dextrins produced by β -amylase were of high molecular weight, whereas those produced by α -amylase were of low, consisting apparently often of only from three to six glucose residues.

The increase in amylase activity observed during the germination of the cereal grains has given rise to much speculation. Early suggestions that the increase was due to the actual synthesis of enzymes have been shown to be erroneous and more modern theories involve the presence of an activator—the amylo-kinase of E. Waldschmidt-Leitz and A. Purr⁸—formed as germination proceeded; but this possibility has not found general acceptance. T. Chrzaszcz and J. Janicki⁹ proposed the exact opposite of this when they suggested that an inhibitor—sisto-amylase—was present and that the protein breakdown products formed during germination counteracted the effects of the inhibitor, whereby the amylase was restored to maximum activity. Eluto-substances such as peptone and sodium chloride had the same effect, namely, increase in amylase activity. It was later shown that the amylase might be inactivated by adsorption on protein and that the addition of peptone had a protective effect on the amylase. The possibility of an inactive protein-amylase complex was indicated by J. S. Ford and J. M. Guthrie as long ago as 1908,¹⁰ when it was shown that an addition of papain to barley extracts caused a large increase in amylase activity. More recently K. Myrbäck and S. Myrbäck¹¹ differentiate between the free amylase in an aqueous extract of barley and the bound amylase which is only liberated after papain digestion. The great increase in β -amylase activity was assumed to be due to the proteo-

⁸ *Z. physiol. Chem.*, 1931, **203**, 117.

⁹ *Biochem. Z.*, 1933, **263**, 250; **264**, 192; **265**, 260.

¹⁰ *J. Inst. Brew.*, 1908, **14**, 61.

¹¹ *Biochem. Z.*, 1933, **258**, 158.

lytic release of insoluble amylase bound in some manner with protein, and such a view is now confirmed by T. Chrzaszcz and J. Sawicki,¹² who find that papain and other proteolytic enzymes, and hydrogen sulphide, liberate bound amylase, which is chiefly of the β -amylase type, since the saccharifying power of such treated extracts is much increased. C. H. Hills and C. H. Bailey¹³ review the present position and have failed to confirm the presence of amylokinase in green malt extracts of barley; they regard the increase of the β -amylase activity after papain digestion as a proteolytic breakdown of a protein complex, and consider that this process provides a satisfactory means of determining total β -amylase activity. Peptone did not affect the β -amylase activity, but increased α -amylase activity by about 25%, in the case of green malt extract and of purified α -amylase solutions. No explanation of the increase in α -amylase activity by peptone is yet advanced.

A minor point of controversy in the constitution of starch has been settled by the outcome of experiments on the yield of carbon dioxide obtained by an improved decarboxylation technique applied to polysaccharides and sugars. It has been observed by several workers in the past that small yields of carbon dioxide were obtainable from starch and cellulose, and the question arose as to whether uronic acid residues in small amount were present in the polysaccharide molecule, or whether such existed in an adventitious impurity. The result of the most recent determinations by W. G. Campbell, E. L. Hirst, and G. T. Young,¹⁴ employing a modified apparatus of the type suggested by A. D. Dickson, H. Otterson, and K. P. Link¹⁵ and conducting the determination in an atmosphere of nitrogen, shows that starch, cellulose and the naturally occurring sugars such as maltose, glucose, galactose, sucrose, etc., all yield amounts of carbon dioxide, averaging about 0.5%, which is obviously not due to the original presence of uronic acids and in the case of the above polysaccharides has no structural significance. In polysaccharides where uronic acids are definitely known to be present, it is obvious that these findings must in future be taken into account, although the correction may be difficult to apply accurately. For the same reason, many of the published figures for uronic acid content must be somewhat too high.

Pectin.—The nature and constitution of pectin and its congeners still remain matters for further experiment and speculation. The older views of Ehrlich, involving a ring structure of four carbohydrate residues, were never in keeping with present views on polysaccharide structure, which have developed almost concurrently

¹² *Enzymologia*, 1937, **4**, 79.

¹³ *Cereal Chem.*, 1938, **15**, 273.

¹⁴ *Nature*, 1938, **142**, 913.

¹⁵ *J. Amer. Chem. Soc.*, 1930, **52**, 775.

with the work of Ehrlich on pectin. Such views are giving way now before the results of more recent work, which tends to bring pectin much more in line with other polysaccharides. The work of Link *et al.*^{16, 17} from 1934 onwards, based on the results of methylation of pectin derivatives similar to those investigated by Ehrlich, and on viscometric and X-ray measurements, indicated that chain formation of galacturonic acid units provides at least the basis of pectic substances. Further support for the uronic acid chain has been forthcoming as a result of the experiments of G. Schneider¹⁸ and co-workers, who approached the problem from a slightly newer angle. They prepared nitro-pectin and found that the product contained two nitro-groups for each galacturonic acid unit; in its physical properties—formation of thin films, viscosity, etc.—it resembled cellulose nitrate. The molecular weight, based on viscosity measurements, varied between 20,000 and 50,000 according to the origin of the product and its method of preparation. From a similar examination of the pectin esters these authors conclude that the essential pectin molecule is built up of a chain of galacturonic acid residues, the carboxyl groups being free, a large proportion being esterified with methyl alcohol. Galactose and arabinose are regarded as impurities and not essential constituents of the molecule.

Whilst arabinose as araban is a recognised concomitant impurity associated with most pectins as prepared in the laboratory, the position of galactose is not quite so clear. F. W. Norris and C. E. Resch¹⁹ have prepared pectins from a number of plant sources, including the flower of the hop, and it is by no means clear from the results of analyses of the products whether galactose may be regarded as an essential constituent or not. The substance known as pectic acid, which corresponds to a completely demethylated pectin, was formerly thought to be a chemical entity, but it is now shown that it is a mixture which under certain conditions of preparation approaches constant composition. By suitable methods of preparation, the araban content of pectin may be reduced to negligible amounts, but so far as is known it is not possible to separate the galactan fraction, nor is the precise nature of this portion known. Even assuming that the basal molecule of pectin is a galacturonic acid chain, the substance isolated in the laboratory is a much more complex product than this, and many of the properties of pectin substances depend on the presence or absence of groups or units which may or may not be part of the molecule. An accurate

¹⁶ *J. Biol. Chem.*, 1934, **105**, 15.

¹⁷ *Ibid.*, 1935, **109**, 293.

¹⁸ *Ber.*, 1936, **69**, 309, 323, 2537, 2541; 1937, **70**, 1611, 1617.

¹⁹ *Biochem. J.*, 1937, **31**, 1945.

definition of the term pectin is lacking at present; if the power to form jellies in acid-sugar mixtures is to be accepted as a criterion, then many so-called pectins must be excluded from the class, since they will be found not to give such jellies. Indeed, beet pectin, which was employed as a typical pectin by Ehrlich, will not form jellies. Schneider correlates jellying power with chain length: pectins from vegetable sources in general are assumed to have short chains and low jellying power; pectins from fruits, especially citrus fruits, have a long chain and corresponding high jellying power. It will be seen, then, that according to this theory jellying power is associated with high molecular weight.

Confirmation of the high molecular weight of citrus pectins in particular, and of fruit pectins in general, is forthcoming from the application of ultracentrifugal methods. T. Svedberg and N. Gralen²⁰ point out that cellulose, starch and glycogen give polydisperse systems in solution which do not possess well-defined molecular weights, and the semi-solid proteins behave similarly. On the other hand the proteins of the body fluids show well-defined molecular weights and it is argued from this that it is to be expected that the carbohydrates of plant juices would behave similarly. The largest proportion of carbohydrate in plant juices is pectin; in bulb and tuber juices regular polysaccharides predominantly occur. Solutions of pectin from fruits were not monodisperse, but were better defined than starch or cellulose solutions. By sedimentation methods, orange pectin was found to have the highest molecular weight (40,000—50,000), and that of apples, pears and plums ranged from 25,000 to 35,000. There is thus substantial agreement on the probable molecular weight whether obtained by sedimentation methods or by the methods adopted by Schneider.

The carbohydrates of bulb and tuber juices proved to be more nearly monodisperse in sedimentation and diffusion. The carbohydrate from the *Lilium* bulb had a molecular weight of 16,000. It was also observed, with potatoes, that the changes undergone by the plant as it develops are reflected in the sedimentation curves. Two well-defined components of high molecular weight may be distinguished even in the early stages of sprouting, and, as growth activity increases, the presence of these components becomes increasingly well marked. It is thought that this is an indication that the reserve carbohydrate passes through two intermediate stages before products of low molecular weight are formed.

In the present uncertain state of knowledge of the precise nature of pectin it is not surprising that definite information with regard

²⁰ *Nature*, 1938, **142**, 261.

to the enzymes responsible for pectin breakdown is not yet available. Much work has been done, and a number of enzymes have been indicated as taking part in the stepwise degradation of pectin to its simpler components. One of these is to be regarded as effecting the removal of methoxyl groups from the pectin, and Z. I. Kertesz²¹ gives details for measuring this pectin-methoxylase activity. The extent of demethylation in slightly alkaline solution increases with the amount of enzyme added, and decreases with increasing concentrations of pectin.

The above author has also provided a review²² of the present state of knowledge of the pectic enzymes.

Cultures of *B. carotovorus* have been largely used as a source of the hydrolytic enzyme pectinase and the effect of variations in the medium on pectinase production has been studied by M. Fernando.²³ The optimum p_H at which the enzyme acts is altered according to whether the medium is acid or not; where acidity of the medium obtains, the optimum p_H changes to the acid side. By growth comparison it was shown that active pectinase is produced more freely in alkaline than in acid conditions, and good enzyme production is effected under conditions which favour the rapid multiplication of the organism.

Hemicelluloses, etc.—The hemicellulose from cottonseed hulls was found by E. Anderson and S. Kinsman²⁴ to contain glycuronic acid, xylose and an unknown substance which they called "body X," now thought to be a dark-coloured condensation product of lignin and furfuraldehyde—an artefact of hydrolysis. The subject has been re-investigated by E. Anderson, J. Hechtman, and M. Seeley,²⁵ who separate two hemicelluloses from the alkaline extract of the hulls by differential precipitation with acid and alcohol, and remove the contaminating body X by successive chlorinations, or preferably brominations, whereby the hemicelluloses are obtained as white powders. The hemicelluloses are mixtures containing only xylose and glycuronic acid in proportions of 1 molecule of acid to 10 to 16 molecules of the sugar.

Hemicelluloses of a somewhat similar type, but containing glucose in addition to xylose and glycuronic acid, were described by S. Angell and F. W. Norris,²⁶ who extracted them from the flower of the hop. This is believed to be the first description of hemicelluloses of floral organs, and it was rather surprising to find that the hemicelluloses were of the xylan type usually associated with highly

²¹ *J. Biol. Chem.*, 1937, **121**, 589.

²² *Ergebn. Enzymforsch.*, 1936, **5**, 233.

²³ *Ann. Bot.*, 1937, **1**, 727.

²⁵ *Ibid.*, 1938, **126**, 175.

²⁴ *J. Biol. Chem.*, 1931, **94**, 39.

²⁶ *Biochem. J.*, 1936, **30**, 2159.

lignified tissues; in the case of hops, however, considerable amounts of lignin are present. The carbohydrates of the bark of trees have not been studied so much as those of the wood, and differences in constituents are indicated by results obtained by H. W. Buston and H. S. Hopf²⁷ for the bark of ash (*Fraxinus excelsior*). The content of pectic substance was higher than that usually encountered in woods, where it is normally present to but a slight extent, and in this case was about 7%. The content of hemicellulose was of the order of 20%, but the nature of this constituent recalled rather the hemicelluloses of leaves than of wood, since galactose was the predominant product of hydrolysis together with galacturonic acid and smaller amounts of mannose and arabinose. The hemicellulose of the bark presented a striking contrast to that of the wood, which contained some 60% of xylan.

The carbohydrate and other constituents of the pericarp of the hazel nut (*Corylus avellana*) have been examined by J. G. Boswell,²⁸ who compares his results with those of D. F. J. Lynch and M. J. Goss²⁹ for the hull of the peanut (*Arachis hypogaea*) and his own for the shell of the Brazil nut (*Bertholletia excelsa*).³⁰ Fractions soluble in benzene, alcohol, water and 4% sodium hydroxide solution were examined, and the contents of cellulose and lignin determined. In addition to chlorophyll the benzene-soluble fraction probably contained a wax; and a phlobatannin was probably present in the alcohol-soluble portion. The water-soluble substances were negligible, but the alkaline extract contained three fractions of hemicellulose-like nature together with lignin. The predominant hydrolysis product was xylose with smaller quantities of uronic acid and methoxyl. The results with hazel nut and peanut showed a similarity in keeping with their morphological identity, and both differ from those obtained for the brazil nut shell, which is a seed coat. It is suggested that, although lignification follows the same general plan in both types of tissue, different processes or factors are at work in the case of the lignified seed coat.

Proteins.—A review of the abstracted literature for the last year shows an apparent lack of great activity where plant proteins are concerned. Amongst publications which may be mentioned is one by N. F. Burk,³¹ who continues, in the case of gliadin, investigations which have been proceeding for some years on the osmotic pressure, molecular weight and stability of plant proteins. The author recalls that Sørensen suggested that gliadin amongst many other proteins is composed of reversibly dissociated systems of components.

²⁷ *Biochem. J.*, 1938, **32**, 44.

²⁸ *Ibid.*, p. 986.

²⁹ *Ind. Eng. Chem.*, 1930, **22**, 903.

³⁰ *Biochem. J.*, 1936, **30**, 971.

³¹ *J. Biol. Chem.*, 1938, **124**, 49.

N. F. Burk and D. M. Greenberg³² had already shown that urea solution involved the dissociation of some proteins into definite units of lower molecular weight, and N. F. Burk³³ has more recently shown that excelsin has a molecular weight of about 212,000 in aqueous salt solution, which is reduced to 35,700 in urea solution. In the case of gliadin osmotic measurements on five preparations in urea solution showed more or less regular variations according to precipitation temperature, and thus demonstrated the non-homogeneous character of the protein. Gliadin is, however, more stable in urea solution than excelsin and certain other proteins, as there was little difference in molecular weight of the protein whether in alcohol or urea solution. It was found that, if the gliadin had been coagulated to some extent by alcohol, such coagulated preparations did give a lower molecular weight in urea solution, and the differing molecular weights indicated for the five preparations above are probably due to the presence in them of varying amounts of coagulated protein. It is also considered that gliadin is denatured by urea, disulphide linkages being present in urea solution, but thiol groups are absent.

The black bean, a variety of *Phaseolus vulgaris*, has an interest in addition to the purely chemical, in that together with maize it comprises almost the entire diet of the Mayas. The proteins of the bean have been recently studied by D. Breese Jones, C. E. F. Gersdorff and S. Phillips,³⁴ who find that the chief proteins are an α - and a β -globulin. They contain relatively large amounts of lysine, tryptophan, histidine and cystine, are closely similar in composition to proteins of other varieties of *Phaseolus*, and with regard to the dietary indicated above are ideal in that the amino-acid composition is supplemental to that of the maize proteins.

The enzyme papain, a representative of plant proteolytic enzymes, continues to attract the attention of investigators. The presence of natural activators in unpurified preparations of the enzyme is generally recognised and their source lies in the latex of *Carica papaya*, wherein the presence of glutathione and other thiol compounds is reported by C. V. Ganapathy and B. N. Sastri.³⁵ The suggestion that glutathione is an activator is contrary to the views, amongst others, of W. Grassmann,³⁶ who postulates a phytokinase which is not glutathione but a dipeptide of cyst(e)ine and glutamic acid. In a later communication C. V. Ganapathy and B. N. Sastri³⁷ endeavoured to establish the activation as a

³² *J. Biol. Chem.*, 1930, **87**, 197.

³⁴ *Ibid.*, 1938, **122**, 745.

³⁶ *Biochem. Z.*, 1935, **279**, 131.

³³ *Ibid.*, 1937, **120**, 63.

³⁵ *Current Sci.*, 1938, **6**, 330.

³⁷ *Nature*, 1938, **142**, 539.

function of the form of sulphur present by treating fresh latex with hydrogen peroxide to oxidise all $-SH$ groups to the $-S-S-$ form, and prepared the product in a dry state. The substance was inactive towards peptone, but retained its action on gelatin; it was in fact as active in this respect as when activated by hydrogen cyanide or glutathione. It was most active at about p_H 3, that is, in far more acid medium than usually reported for papain; maleic acid had little effect on activity, but iodoacetic acid produced an irreversible inactivation. These results would suggest that the presence of $-SH$ groups is unnecessary for gelatinase activity, but essential for peptonase activity, and it is argued that possibly the hydrolysis of protein by papain takes place in two stages: first to peptone and then to amino-acids, the activation mechanism being specific for the two stages.

The nature of the activation mechanism has also been studied by M. Bergmann and J. S. Fruton,³⁸ who find that, although phenylhydrazine will activate unpurified preparations of papain which contain the natural activators, it is without action on purified specimens. Substrates such as benzoylarginineamide, albumin and peptone were used and in each case the activating action of phenylhydrazine was restored by addition of hydrocyanic acid to the purified preparations.

A study of the papain-amylase complex by S. Akabori and K. Kasimoto³⁹ has led to the preparation of more highly active papain preparations than the original product used. From the complex in acetate buffer solution, the amylase is removed by alumina, leaving the papain some 10–20 times more active. It was found by S. Okomura,⁴⁰ however, that the preparation on these lines coagulated readily and a more satisfactory preparation was obtained by him after alumina adsorption, by saturating the solution with ammonium sulphate, dialysing, and precipitating with acetone. Thiol groups were absent from the preparation, which hydrolysed gelatin more rapidly in presence than in absence of hydrocyanic acid.

Pigments.—The flowers of *Gazania rigens* provide a rarity in that most of the carotenoids present belong to the γ -carotene series. In the fifth contribution to a series of papers on the carotenoids, K. Schön⁴¹ describes a new xanthophyll, gazaniaxanthin, which contains one atom of oxygen and is of probable formula $C_{40}H_{54}O$ or $C_{40}H_{56}O$. The new xanthophyll was obtained by chromatographic analysis of the saponified lipid extracts of the flowers. There is an upper zone of rubixanthin and a large colourless zone separating

³⁸ *Science*, 1937, **86**, 496.

³⁹ *Bull. Chem. Soc. Japan*, 1938, **13**, 453.

⁴⁰ *Ibid.*, p. 534.

⁴¹ *Biochem. J.*, 1938, **32**, 1566.

this from the second coloured zone, which contains the gazanixanthin, accompanied by another unknown and difficultly separable carotene. Finally, there is a small zone of γ -carotene. The structure of gazanixanthin is not yet known; it yields an acetyl derivative on treatment with acetic anhydride in pyridine solution, whereby the presence of one alcoholic hydroxyl group is inferred. It is tentatively suggested that it may be an isomeride of rubixanthin, the hydroxyl being in the aliphatic side chain as in lycoxanthin and lycophyll. An interesting consequence of such a suggestion is that the substance, unlike rubixanthin, would then be active as a provitamin A, and biological tests would therefore decide this structural consideration.

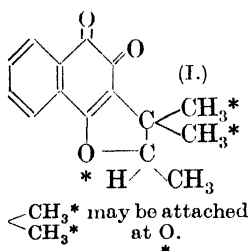
A new xanthophyll is also reported by H. H. Strain,⁴² who finds that in ester form it is the principal pigment present in the petals of the Californian poppy. He calls the pigment eschscholtzianthin after the botanical name of the plant and, as obtained by saponification of the esters, it has the empirical formula $C_{40}H_{54 \pm 2}O_2$. The molecule is highly unsaturated, containing twelve double bonds, possibly in a single conjugated system, and two hydroxyl groups. The pigment and its esters are more unstable than the common carotenoids, a fact which causes difficulties in the preparation; thus, they are easily affected by heat, as indicated by changes in the spectral absorption properties. Similarly, they take up oxygen much more readily from the air; the rate of oxidation in different solvents varies but is not increased in the presence of hæmin, as has been reported in the case of lycopene.

Apparently the large green-yellow fruit of *Maclura pomifera* Raf. known as the osage orange, growing widely in parts of Oklahoma and Texas, has largely escaped the attention of the chemist. The yellow pigment has, however, been isolated recently by E. D. Walter, M. L. Wolfrom, and W. W. Hess,⁴³ who have obtained as much as 6% on the dry weight of the fruit. The pigment is soluble in organic solvents in general, but not in light petroleum, a fact which is made use of in its preparation. The dried and powdered fruit is extracted exhaustively with light petroleum and then with ethyl ether, from which solvent the pigment may be recovered and then recrystallised from xylene and alcohol. Evidence of structure is not yet complete, but the product appears to be an *o*-dihydric phenol and a lactone structure is indicated. It gives a mono- and a di-acetate, the second acetyl group being saponified only with difficulty; the name osajin has been suggested and the provisional formula in accordance with present findings is $C_{24}H_{22}O(CO \cdot O)(OH)_2$.

⁴² *J. Biol. Chem.*, 1938, **123**, 425.

⁴³ *J. Amer. Chem. Soc.*, 1938, **60**, 574.

A new colouring matter belonging to the naphthalene group is the subject of a preliminary communication of J. R. Price and



R. Robinson.⁴⁴ The name dunnione is suggested for the pigment, which occurs as deposits on the leaves of *Streptocarpus Dunnii* Mast. and appears to be a derivative of β -naphthaquinone of empirical formula $C_{15}H_{14}O_3$. The third oxygen atom is a member of a coumaran ring, and the general chemical and physical properties and its degradative reactions lead to the conclusion that it is 2 : 3 : 3-trimethyl-6 : 7-benzo-

coumaran-4 : 5-quinone (I). This colouring matter is different from, but possibly related to, colouring matters described by S. Siddiqui,⁴⁵ which were obtained from the reddish dust on leaves of *Didymocarpus pedicellata*.

The red pigment of the beet, which was first isolated by G. Schudel⁴⁶ and has since been examined by A. D. Ainly and R. Robinson,⁴⁷ is the subject of a communication by G. W. Pucher, L. C. Curtis, and H. B. Vickery,⁴⁸ who describe in the first instance a method of preparation of the unstable pigment. The method is based on the fact that most of the pigment may be obtained in the precipitate formed when the dried tissue is extracted with acid alcohol, and the extract subsequently neutralised with lithium hydroxide. The dried concentrate contains 16% of pigment and the latter may be obtained, after lead treatment, in ill-defined crystalline form, which has a constant extinction coefficient (Zeiss spectrophotometer). Although formulation is not possible on the evidence so far obtained, betanin is undoubtedly a glycoside of a nitrogenous nucleus, which appears to be closely related to the anthocyanidins. The form in which the nitrogen is present is not known yet with certainty; aliphatic amino-groups are unlikely, aromatic amino- or ring nitrogen is possible. The authors also describe a method of determination of betanin based on a knowledge of the extinction coefficient of the pure substance at definite concentration when viewed through the S 53 filter of the Zeiss instrument.

The survey of anthocyanins, commenced by R. Robinson *et al.* (1931 onwards), is taken up by J. R. Price and V. C. Sturgess,⁴⁹ who have examined 200 species in 110 genera with respect to the nature

⁴⁴ *Nature*, 1938, **142**, 147.

⁴⁵ *J. Indian Chem. Soc.*, 1937, **14**, 703.

⁴⁶ *Dissert.*, Zürich, 1918.

⁴⁷ *J.*, 1937, 446.

⁴⁸ *J. Biol. Chem.*, 1938, **123**, 61, 71.

⁴⁹ *Biochem. J.*, 1938, **32**, 1658.

of the anthocyanins of the young leaves. The anthocyanin coloration of young leaves which disappears on reaching maturity is probably a more general phenomenon than the more obvious familiar autumnal coloration, and a wide range of plants has been examined. The great majority—93%—of the pigments were cyanidin saccharides, and half of these were pentose glycosides, about 30% in each case were monoglycosides and 3-biosides, with a small remainder of 3 : 5-dimonosides.

In a later communication on the same subject, W. J. C. Lawrence, J. R. Price, G. M. Robinson, and R. Robinson⁵⁰ indicate new points in the technique of examination designed to overcome the difficulties in determining glycoside type involved in the presence of a number of substances such as tannins and anthoxanthins. As in the young leaves, the autumn leaves showed a great preponderance of cyanidin saccharides, but owing to the interference of foreign substances of the type indicated the results with regard to sugar type are not so conclusive as in the case of young leaves, where interfering substances gave less trouble.

Finally, J. R. Price, V. C. Sturgess, R. Robinson, and G. M. Robinson⁵¹ have summarised the results of recent surveys of anthocyanins, and forecast interesting future possibilities. The anthocyanins of angiosperms show an overwhelming predominance of pigments based on pelargonidin, cyanidin and delphinidin and methyl ethers of the last two. New types are exemplified by the nitrogenous pigment of the beet already discussed and by gesnerin from the flowers of *Gesnera fulgens*; the yellow pigment of the Iceland poppy is also nitrogenous. The new types of anthocyanin have been found in the *Pteridophyta*; they consist of monoglycosides and diglycosides, and the corresponding anthocyanidins do not correspond to the common types already established; they are probably based on 6-hydroxypelargonidin and 6-hydroxycyanidin.

An interesting point is raised by D. Erikson, A. E. Oxford, and R. Robinson,⁵² who discuss the occurrence of anthocyanins in bacteria, and draw the conclusion that this has not so far been established despite the numerous references to such in the literature and in text-books. It is pointed out that the evidence for their existence is not satisfactory or complete, since there is no example of the isolation and complete characterisation of an anthocyanin from such a source. Many classes of basic dyes—the oxazines, thiazines and azines—contain a heterocyclic nucleus associated with hydroxylated benzene rings and would simulate the indicator reactions of anthocyanins. Moreover, the flavylum nucleus will

⁵⁰ *Biochem. J.*, 1938, **32**, 1661.

⁵¹ *Nature*, 1938, **142**, 356.

⁵² *Ibid.*, p. 211.

not withstand treatment with boiling aqueous alkali, whereas a pigment from *Actinomyces Waksmanii*, described as an anthocyanin by A. E. Kriss,⁵³ gives a stable royal-blue colour after such treatment. The latter pigment thus probably belongs to one of the more stable types suggested above.

Chemical Aspects of Some Micro-organisms.

Aspergillus.—In papers dealing with the intake of nitrogen as nitrates by *A. niger*, D. Itzerrott⁵⁴ and E. Bünning⁵⁵ are in agreement that the effect of the p_H of the substrate does not lie in its influence on the charge on the colloids of the plasma or on the permeability of the cell membrane to nitrate molecules. Accumulation of nitrate ions occurs when the substrate is more acid than p_H 3, but the nitrate is not utilised under these conditions. With decrease in acidity, part of the accumulated nitrate disappears. Assimilation of nitrogen as ammonium ions also increases with increasing alkalinity, but is not entirely inhibited by acid conditions as in the case of nitrate. The latter author also discusses the intake of dyes by the organism and finds that the rate of intake is conditioned by the concentration of dyes within the cell. Such concentration depends on the adsorptive power of the sap colloids, and this is controlled by the p_H of the substrate. Increasingly acid substrates tend to increase the concentration of basic dyes and to decrease that of the acid dyes.

The utilisation of various forms of nitrogen by *A. niger* with special reference to the supply of essential metallic salts has been investigated by R. A. Steinberg,⁵⁶ who finds that ammonium and nitrate ions and the nitrogen of urea and asparagine are equally utilised, provided that such metallic salts are present. In particular, zinc, copper, manganese and molybdenum in suitable amount are necessary for satisfactory nitrogen uptake and the importance of the last element is stressed. It was found that more molybdenum was necessary when nitrogen was presented as nitrate than for other forms, and it is suggested that molybdenum is required in respect of the activity of the nitrate-reducing enzyme system.

The influence of certain heavy-metal salts on the composition of *A. niger* has been shown by G. Schulz⁵⁷ to vary with the strain and age of the culture. The formation of higher carbohydrates is favoured, and that of lignin and its congeners inhibited by the presence of manganese, cadmium, iron and zinc. Fat formation also is influenced by the metals indicated, manganese and iron

⁵³ *Compt. rend. Acad. Sci. U.R.S.S.*, 1936, **4**, 283.

⁵⁴ *Flora*, 1936, **31**, 60.

⁵⁵ *Ibid.*, p. 87.

⁵⁶ *J. Agric. Res.*, 1937, **55**, 891.

⁵⁷ *Planta*, 1937, **27**, 196.

stimulating, and zinc and cadmium retarding production. Salts of all four metals increase the production of metabolites, but show considerable differences individually in the extent of stimulation which they induce.

In the twelfth part of a series of investigations on the chemistry of mould tissue, D. W. Woolley and W. H. Peterson⁵⁸ identify histidine, lysine and arginine in the mycelium of *A. sydowi*. The first two are isolated from the autolysate, but arginine undergoes destruction during autolysis and is probably present in combined form. It may, however, be obtained in the aqueous extracts of the fresh tissue. The minimum amounts of the acids found are small, representing little more than 5% of the total nitrogen of the mycelium.

In the next communication⁵⁹ of the series, some 17% of the nitrogen of the mycelium had been accounted for as definite compounds. The amino-acids of the autolysate now include predominantly leucine and serine, and dicarboxylic acids, proline, tryptophan, tyrosine, isoleucine and valine are also present. The authors were unable to detect alanine, glycine, phenylalanine and hydroxyproline.

Finally, in the latest communication⁶⁰ to date, an acetone extract of the fat-free mycelium or the usual autolysate has been found to contain cyclic choline sulphate.

The zymase system of enzymes which is responsible for normal alcoholic fermentation is shown to occur in various species of *Aspergillus* and *Penicillium* by T. G. Tomlinson,⁶¹ who finds, for example, that *A. niger* cultured in peptone is able to convert sugar into alcohol under anaerobic conditions. Two penicillia, *P. divaricatum* and *P. sanguifluus*, produce, in presence of calcium carbonate, citric acid and alcohol, but the former is produced more rapidly than the latter, and there appears to be no relation between citric acid production and the presence of zymase.

An increase in the production of citric acid from sugar, and of oxalic acid from acetic acid, is claimed by V. S. Butkevitch and E. I. Trofimova⁶² when the mycelium of *A. niger* is removed from the normal nutrient medium and placed for 24 hours in aqueous magnesium sulphate solution.

New Metabolites.—In a continuation of studies on the biochemistry of micro-organisms, J. N. Ashley and H. Raistrick⁶³ describe two new metabolic products isolated from the mycelium of *Helmintho-*

⁵⁸ *J. Biol. Chem.*, 1937, **118**, 363.

⁵⁹ *Ibid.*, 1937, **121**, 507.

⁶⁰ *Ibid.*, 1938, **122**, 213.

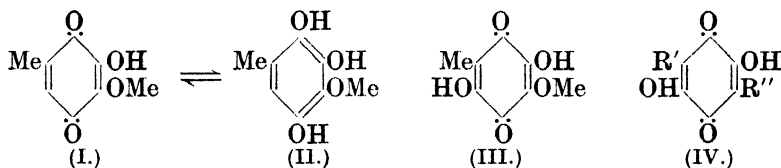
⁶¹ *New Phytol.*, 1937, **36**, 418.

⁶² *Compt. rend. Acad. Sci. U.R.S.S.*, 1937, **17**, 221.

⁶³ *Biochem. J.*, 1938, **32**, 449.

sporium leersii. These are present in considerable quantity and are chemically similar, the names luteoleersin and alboleersin being suggested. As the names imply, the former is a yellow substance, the latter white; they have both been obtained in crystalline form and bear the chemical relationship of a substituted quinone or semiquinone and its corresponding phenol. Thus, luteoleersin is readily reduced to alboleersin, and the opposite change is effected by simple oxidation. Derivatives were not obtained in crystalline form, since a number of attempts to methylate, acetylate and benzoylate the substances yielded products of a gummy or glass-like nature. The simple relationship between the two substances suggests that they may comprise an oxidation-reduction system in the life-process of the organism.

Another pair of metabolic products, which also probably comprise an oxidation-reduction system in *A. fumigatus*, is described by W. K. Anslow and H. Raistrick.⁶⁴ The metabolism solution of this fungus was observed to change in colour from yellowish-brown to purple when made alkaline, and the substance responsible was shown to be a new product, fumigatin. This was found to be 3-hydroxy-4-methoxy-2:5-toluquinone (I), and it was readily interconvertible with its reduction product, 3-hydroxy-4-methoxytoluquinol (II). A further interest attaches to these products in that it has now been possible to convert fumigatin *in vitro* into a metabolic product of *Penicillium spinulosum*, now named spinulosin (III). The latter now appears as 3:6-dihydroxy-4-methoxy-2:5-toluquinone, or 6-hydroxy-fumigatin. The formulæ of these compounds recall several naturally occurring derivatives of 2:5-dihydroxy-1:4-benzoquinone, such as embelin (IV; R' = H, R'' = *n*-lauryl) and pyropic acid (IV; R' = R'' = phenyl).



As this Report goes to press a further communication by W. K. Anslow and H. Raistrick⁶⁵ appears, in which they report the isolation of spinulosin from cultures of a strain of *A. fumigatus*. This is in contrast with the previous finding that from another strain of the same organism fumigatin only was produced. Thus, two strains of the same species give rise to different metabolites, and, further, since spinulosin was originally obtained from

⁶⁴ *Biochem. J.*, 1938, **32**, 687.

⁶⁵ *Ibid.*, p. 2288.

P. spinulosum, yet another example of the same metabolite from two different genera is afforded.

Proteolytic Enzymes of Bacteria.—Of recent investigations on bacterial proteinases may be mentioned those of G. Gorbach, who with E. Pirch⁶⁶ has shown that *B. fluorescens* and *B. pyocyaneus* excrete into the culture medium a proteinase whose optimum p_H is 7. A peptidase operating at p_H 8.4 was shown to be present in the cells. The proteinase was later shown to be a product of the autolysis of dead bacteria.⁶⁷ G. Gorbach⁶⁸ was also able to separate from cultures of *Caseiococcus* and *Gastrococcus* a proteinase of the papain type which had an optimum p_H of 4.7, as distinct from the common bacterial proteinase, whose optimum p_H , as above, was 7. The separation was effected by dialysis with diammonium hydrogen phosphate.

The view that bacterial proteinases belong to neither the papain nor the tryptase group, but constitute an intermediate group, is advanced by E. Maschmann,⁶⁹ who has examined the proteolytic activity of culture filtrates of a number of strains of *B. prodigiosus*, *pyocyaneus* and *fluorescens liquefaciens*. Activators, such as cysteine, reduced glutathione, hydrocyanic acid, ascorbic acid, chloroacetic acid and potassium ferrocyanide, are without activating action on the filtrates, nor do they activate the proteinase solutions free from peptidase prepared from them. The proteinases prepared from the different culture filtrates were probably identical, and were effective in hydrolysis of gelatin and clupeine at p_H 7.

However, activating agents are effective with some bacterial proteinases, as shown in an investigation of the proteinase of *Clostridium histolyticum* by L. Weil and W. Kocholaty,⁷⁰ who employed the bacteria-free filtrates from anaerobic cultures. The enzyme was extracellular and operated best at p_H 7.0. Thiol compounds activated the enzyme and the activation was itself catalysed by heavy-metal ions. In the presence of cysteine and ferrous ions, the activation was maximal under anaerobic conditions. As the growth of the cultures increased, proteinase activity also increased up to a maximum in 24 hours, followed by progressive decrease after that period. Moreover, somewhat similar results were later obtained by E. Maschmann,⁷¹ using *Bacillus perfringens*, *Vibrio septicus* and *B. botulinus*. It was found that the first-named organism yielded small amounts of di- and aminopoly-peptidase, and larger amounts of an enzyme which hydrolysed gelatin, and another enzyme which on activation by thiol compounds such as

⁶⁶ *Enzymologia*, 1936, **1**, 191.

⁶⁷ *Ibid.*, 1937, **2**, 92.

⁶⁸ *Ibid.*, 1937, **3**, 65.

⁶⁹ *Biochem. Z.*, 1937, **294**, 1.

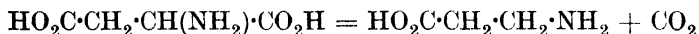
⁷⁰ *Biochem. J.*, 1937, **31**, 1255.

⁷¹ *Biochem. Z.*, 1937, **295**, 1.

cysteine and reduced glutathione or, to a less extent, by hydrocyanic acid, hydrolysed clupeine. *Vibrio septicus* yielded a closely similar mixture of enzymes, as also did *B. botulinus*, but in the latter case the protease was able to hydrolyse native protein such as caseinogen and fibrin in addition to gelatin.

The subject of bacterial proteinases has also been taken up by J. Berger, M. J. Johnson, and W. H. Peterson,⁷² who communicate the first of a series of papers in which the peptidases of *Leuconostoc mesenteroides* are described. In some cases the presence of acidopeptidases from bacterial autolysates has been demonstrated. The complex of peptidases obtained appears to consist of at least six enzymes, including two dipeptidases, three polypeptidases and an acylase; but no carboxypeptidase was found. Both optical components of a number of racemic peptides were hydrolysed by *Leuconostoc* peptidases, such peptides including leucylglycine, alanylglycine, and the diglycyl peptides of alanine and leucine. A number of metallic ions were capable of producing an activating effect in some of these hydrolyses.

The conversion of *l*-aspartic acid into β -alanine has been shown by A. I. Virtanen and T. Laine⁷³ to be accomplished by simple decarboxylation by living legume bacteria :



In collaboration with P. Rintala⁷⁴ they have now shown that such a decarboxylation takes place when a bacterial suspension in toluene is used at p_{H} 7. A similar decarboxylation takes place with *l*-glutamic acid, γ -aminobutyric acid being formed, and in both reactions the change is quantitative. It seems doubtful, however, whether the same enzyme is acting in both reactions, since it has been shown that some plant tissues contain an enzyme which will decarboxylate glutamic acid but not aspartic acid. Hence it is suggested that the legume bacteria may produce two decarboxylating enzymes: glutamic decarboxylase and aspartic decarboxylase.

The deamination of aspartic acid has also been investigated by A. I. Virtanen and J. Erkama,⁷⁵ who precipitate a substance having aspartase and asparaginase action, but not fumarase action, from the cell-free solution of *B. fluorescens liquefaciens*. The following experimental facts were observed with this fumarase-free preparation: malic acid was formed from fumaric acid in the presence of ammonia, in absence or presence of toluene; on

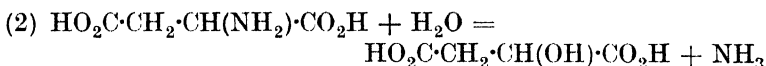
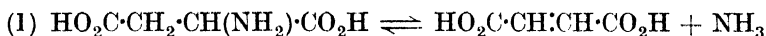
⁷² *J. Biol. Chem.*, 1938, **124**, 395.

⁷³ *Suomen Kem.*, 1937, **B**, **10**, 2; *Enzymologia*, 1937, **3**, 266.

⁷⁴ *Nature*, 1938, **142**, 674.

⁷⁵ *Ibid.*, p. 954.

prolonged action, aspartic acid, malic acid and ammonia only were present in the solution; with aspartic acid as substrate, fumaric acid, malic acid and ammonia were formed. Hence it is concluded that two distinct enzymes are present in the preparation, which catalyse the two reactions below, the first being a true aspartase action :



It is claimed that the latter reaction is probably the first demonstration of a hydrolytic deamination. It is further pointed out that this work represents an advance on that of E. F. Gale⁷⁶ in that, although he separated two deaminases from the aspartase of *B. coli*, both of his preparations contained fumarase, which thus masked the true nature of the mechanism of action.

Bacteria and Carbohydrates.—The first of a series of studies on cellulose-decomposing organisms is published by E. Walker and F. L. Warren,⁷⁷ who have used *Cytophaga Hutchinsoni*, an aerobic organism which is specific for cellulose in the sense that no other carbohydrate is decomposed by it. The products of its action are complex, and under fully oxygenated conditions one half of the cellulose may be decomposed in about eight days. Amongst the non-gaseous products formed is predominantly a mucilaginous substance which appears to be an oxycellulose of acidic type, non-reducing, and yielding xylose amongst other hydrolysis products. About one third of the products is accounted for by this mucilage, together with a yellow pigment—possibly of the nature of an aliphatic acid of rather low molecular weight—a higher fatty acid, and a carbohydrate soluble in 75% alcohol. The remaining two-thirds of the cellulose is accounted for as carbon dioxide, and it is suggested that this large production of carbon dioxide from cellulosic material plays an important part in the return of cellulose to the carbon cycle. It is also suggested that the mucilaginous oxycellulose may possibly represent one of the so-called organic colloids of the soil; it is resistant to bacteria, but sometimes succumbs to the attack of fungi, and its general properties, mode of formation and capacity to hold large volumes of water render it particularly suitable as a humic substance. Decomposition up to 80% of added cellulose is claimed for certain strains of *Sorangium* and *Archangium* by H. and S. Krzemieniewski.⁷⁸ The best source of carbohydrate is cellulose, and normal growth takes place with this sole source,

⁷⁶ *Biochem. J.*, 1938, **32**, 1583.

⁷⁷ *Ibid.*, p. 31.

⁷⁸ *Bull. Acad. polonaise*, 1937, *B*, *I*, 11, 33.

although certain other carbohydrates may be substituted for it. As sources of nitrogen, nitrates are utilised, being reduced, and ammonium salts also; organic nitrogen is not utilised. The products of cellulose degradation appear to be similar in general character to those described in the previous reference; mucilaginous substances are formed, together with fatty substances and pigments.

The action of a number of common pathogenic and non-pathogenic bacteria on sugars and their derivatives has been studied by L. Sternfeld and F. Saunders.⁷⁹ As a general rule it was found that the derivative of a sugar was less likely to be decomposed by any given organism than the sugar itself. Hexoses and pentoses were fermented in most cases, but fewer organisms attacked the latter, and heptoses and octoses were unattacked. Glucononose was attacked by only two bacteria and one yeast which was included in the survey.

Several studies on enzyme formation and polysaccharide synthesis by bacteria have been published recently by E. A. Cooper and his associates. Polysaccharides are formed by *B. mesentericus*, *B. megaterium*, and *Ps. pruni* from sucrose, and *Ac. xylinum* produces polysaccharides from sorbitol; but the synthesis in all cases is inhibited by mannose and arabinose, owing, it is thought, to a toxic action on the cell rather than to inhibition of enzyme action. In most cases, the supply of nitrogen is obtained by use of a peptone medium, but this is not essential, as it has been shown that asparagine may be used as sole source of nitrogen. The bacteria which are pathogenic to plants synthesise polysaccharides from sucrose, and such polysaccharides have been shown to be of fructosan type, no evidence of dextrans or pentosans having been obtained (E. A. Cooper and J. F. Preston).⁸⁰

In the next paper of the series, A. Carruthers and E. A. Cooper⁸¹ find that a fructosan is formed by *B. lactis* from sucrose only. When, however, *Leuconostoc dextranicum* was incubated with sucrose, a dextran was formed, the solution containing fructose; incubation with glucose, however, gave little or no dextran. An acceleration of growth, over and above that due to added nitrogen, was evinced on addition of alcoholic extracts of molasses; dextran formation was likewise increased.

The synthesis of polysaccharides from nitrogen-fixing organisms is the subject of the next paper by E. A. Cooper and J. F. Preston.⁸² A large number of substances yield a gum-like substance, built of glucose and glycuronic acid, when supplied to *Rhizobium radicicolum*.

⁷⁹ *J. Amer. Chem. Soc.*, 1937, **59**, 2653.

⁸⁰ *Biochem. J.*, 1935, **29**, 2267.

⁸¹ *Ibid.*, 1936, **30**, 1001.

⁸² *J. Soc. Chem. Ind.*, 1937, **56**, 1r.

These include mono-, di- and poly-saccharides, polyhydric alcohols of 3, 5 and 6 carbon atoms, and the sodium salts of such acids as lactic and succinic. Similar results were obtained with *Azotobacter chroococcum*, but organisms of this type will not synthesise poly-saccharides in media containing high concentrations of sugars, in contrast to those of the preceding papers above.

Finally, to date, E. A. Cooper, W. D. Daker, and M. Stacey⁸³ describe media for the large-scale preparation of polysaccharides from *Rhizobium* and *Azotobacter* and suggest that these polysaccharides are of the same class as the specific polysaccharides of pneumococcus types II and III.

F. W. NORRIS.

⁸³ *Biochem. J.*, 1938, **32**, 1752.

ANALYTICAL CHEMISTRY.

I. INTRODUCTION.

THE majority of the problems presented to the analyst are not new, and they can usually be solved by standard routine methods. The existence of such methods does not mean, however, that in all cases the answer obtained is adequate. A large proportion of the recent work in Analytical Chemistry has very properly been devoted to modifying current procedure and devising new methods, along classical analytical lines, to give results which more nearly approximate to the truth. The development in this field is now one of detail: the problem, the manipulative technique, even the reactions involved, are often familiar; it is the conditions or the precipitants or the application of a particular reaction that may be new. E. S. Larsen's observation ¹ that the analysis of samples of silicates by a number of commercial analysts showed differences of 2.5% in the determination of silica, titania, and alumina and of more than 4% in lime shows that such development is essential and the field by no means exhausted.

In addition to the problems which classical analysis presents, a new series has arisen. The use of small quantities of rare earths in non-ferrous alloys (*e.g.*, cerium or niobium in aluminium), and of thin films of corrosion-resistant materials, the importance of cobalt and copper in ruminant nutrition, the physiologically essential trace elements, vitamins, hormones—these exemplify the growing complexity which calls for improved methods of attack. The need for increased speed in the analysis of large numbers of routine samples, *e.g.*, metals and soils, has also encouraged progress.

New applications of the evident facts that any property which is characteristic of a material may in principle be used as a qualitative test, and that a quantitative method may be founded on the measurement of any quantity the value of which is dependent upon the amount of material present, have formed the bases of recent developments. Such properties as crystal structure, dielectric constant, or reduction potential, or emission, absorption, fluorescence, and Raman spectra fall within this category.

Progress along these and similar lines has encouraged and in certain cases been dependent upon the development of new techniques, some of which we shall describe. X-Ray, polarographic,

¹ *Amer. J. Sci.*, 1938, **35**, 94.

and absorption-spectra methods have received only brief comment in earlier Reports and these are given due treatment. Electron-diffraction analysis has previously not been mentioned. Problems in the analysis of alkaloids and other drugs, sugars, vitamins, and recent attempts to solve them are recorded. The continued growth of micro-analysis, and the realisation that a micro-method, even if large amounts of material are available for analysis, may often be more accurate than macro-analysis, give added importance to this subject.

Limitations of space have restricted the number of subjects dealt with, and even in the treatment of particular themes direct reference to much work of merit has of necessity been omitted.

2. APPLICATIONS OF X-RAYS.

To Moseley the use of X-rays as an analytical weapon was no more than a possibility. Sixteen years ago that possibility was first realised by A. Hadding,² and since that time X-ray methods have gradually emerged from the tentative stage to the position of recognised practical value which they enjoy to-day.

That the frequencies of X-rays emitted by a target on bombardment with cathode rays are characteristic of the element composing the target is a fundamental property which forms the basis of one analytical method. A second depends upon the fact that primary X-rays from one source may on striking another target give rise to characteristic secondary rays. Absorption of X-rays serves as a third method, and the extensive work on X-ray diffraction has profitably been adapted to give a fourth means of solving analytical problems.

The measurement of the primary spectral emission lines, in which the unknown material served as the target, enabled D. Coster and G. von Hevesy³ to confirm the existence of hafnium and played a predominant part in the discovery of masurium, rhenium, and illinium. Its quantitative possibilities were soon realised, and von Hevesy and his collaborators used the method for the quantitative estimation of hafnium in zirconium, and tantalum in niobium. C. E. Eddy, T. H. Laby, and A. H. Turner⁴ developed the technique, and were able to detect one part of iron in 300,000 parts of zinc. G. R. Fonda,⁵ who used cathode rays which had passed out of the vacuum tube through a window on to the specimen, obtained an

² *Z. anorg. Chem.*, 1922, **122**, 195.

³ *Nature*, 1923, **111**, 79.

⁴ *Proc. Roy. Soc.*, 1929, *A*, **124**, 249; 1930, **127**, 20.

⁵ *J. Amer. Chem. Soc.*, 1932, **54**, 115; G. R. Fonda and G. B. Collins, *ibid.*, 1931, **53**, 113.

accuracy of 2% in the determination of tantalum and niobium in molybdenum. By comparing line intensities of the elements sought for with those of another element (*e.g.*, cerium) present in known amount, K. Kimura ⁶ has determined lanthanum, neodymium, and gadolinium in the presence of other rare earths.

The method is attractive in that the spectra obtained, particularly the *K*-series, are simple in comparison with optical emission spectra and, unlike these, are independent of electrical conditions. That they are equally independent of the chemical combination of the elements and their environment is in general true, though Günther and his co-workers ⁷ observed that a mixture of chromium and copper in the ratio 46 : 54 gave an apparent ratio of 60 : 40 owing to the chromium being excited by the rays emitted by the copper. Dilution of the mixture with ground quartz removed this interference. The danger of the distortion of results due to the effect of an absorption edge on emission lines must also be recognised. If in a mixture one element has a characteristic absorption edge of longer wave-length than the emission wave-length of the constituent, then selective absorption occurs.

Inaccuracies in the first method may also arise from the heating of the anticathode affecting the surface concentration. G. von Hevesy ⁸ avoided this difficulty by the use of secondary rays. The choice of the exciting radiation is important. Characteristic primary rays give fluorescent secondaries many times more intense than those obtained with continuous spectra, and the greatest intensity is obtained when the characteristic rays of the target metal are 0.15—0.20 μ shorter than the absorption bands of the elements undergoing analysis. G. von Hevesy, J. Böhm, and A. Faessler ⁹ have given tables of comparison elements which may be added as calibrating media for the determination of any particular element.

The absorption of X-rays by a screen of the material under investigation has been shown by R. Glocker and W. Frohnmayer ¹⁰ to be governed by the equation $I_2/I_1 = e^{-cp}$, where I_2 is the intensity of radiation leaving the screen on the short wave-length side of the absorption discontinuity, I_1 that on the long wave-length side, c is a constant experimentally determined, and p the amount of the element present. V. Caglioti and P. Agostini ¹¹ employed the measurement of characteristic absorption edges in the analysis of

⁶ *Bull. Chem. Soc. Japan*, 1938, **13**, 10.

⁷ P. Günther and I. N. Stranski, *Z. physikal. Chem.*, 1925, **118**, 257; P. Günther and G. Wilcke, *ibid.*, 1926, **119**, 219.

⁸ "Chemical Analysis by X-Rays and Its Applications" (1932).

⁹ *Z. Physik*, 1930, **63**, 74.

¹⁰ *Ann. Physik*, 1925, **76**, 369.

¹¹ *Atti R. Accad. Lincei*, 1931, **14**, 301.

mixtures of alumina containing 0.2—4% of nickel oxide. F. Voges¹² has discussed improvements in the accuracy obtainable. N. H. Moxnes¹³ used X-ray line absorption. 10^6 G. of nickel in zinc was detected by P. de la Cierva and L. Rivoir¹⁴ by employing the coefficient of weakening through successive films of the blackening due to X-rays to determine the constant in Glocker's formula.

Since the atoms in a crystal are arranged in a regular manner, it is evident that, within the crystal, planes exist which contain large numbers of atoms. If the perpendicular separation for one series of planes is d , then for X-rays striking this series at an angle θ and diffracted at the same angle, equality of phase and therefore reinforcement will occur when $2d \sin \theta = n\lambda$, λ being the wavelength of the incident beam and n an integer. From this fundamental formula the interplanar spacings and hence the structure of the crystal may be calculated. If the diffracting beams are photographically detected, a series of points will be obtained on the plate. A number of partly oriented crystals give spots, then arcs, and finally, when the orientation is completely chaotic, rings are obtained.

X-Ray diffraction methods may be used when the material under investigation is either a single crystal or in the powdered state, but since few substances are conveniently obtainable as single crystals the powder method of Debye and Scherrer and of Hull is more generally employed. An essential condition of the method is that an entirely chaotic orientation of the particles should be obtained, so that enough particles are inclined at the required angle to the monochromatic incident beam to give a strong reflexion from one set of parallel planes, reflexion from another set being produced by other particles inclined at a different angle to the incident beam. Even with powder ground to pass a 200-mesh sieve, it is generally difficult to obtain a sufficiently chaotic arrangement of the crystals of any constituent present to an extent less than 1% by volume, whereas for crystals of low symmetry (*e.g.*, triclinic) a finer state of subdivision may be necessary.

It is inherent in the method that the diffraction patterns produced are dependent on the state of chemical combination of the elements which form the crystal lattice: for example, sodium chloride and potassium bromide can be distinguished from sodium bromide and potassium chloride, a feature the analytical value of which is evident. Both the breadth of the method and its limitations are illustrated

¹² *Z. Physik*, 1933, **80**, 542.

¹³ *Z. physikal. Chem.*, 1929, *A*, **144**, 134; 1931, *A*, **152**, 380.

¹⁴ *Anal. Fis. Quím.*, 1936, **34**, 770.

by the observation ¹⁵ that of 1,000 substances from a typical chemical stores only 50 gave no pattern, some were identifiable at less than 1%, others at less than 10%, and others at less than 50%. The existence of this limit of sensitivity and its numerical value, which in certain cases can be quite high, are determining factors in assessing the utility of the diffraction method for a particular problem.

From the X-ray diffraction pattern of a single material the interplanar spacings may be calculated and the relative intensities of the diffracted beams measured by an ionisation chamber, a Geiger-Müller counter, or more usually, by obtaining a photographic record. Inspection alone enables orders of blackness to be estimated, and this is often sufficient. When greater precision is required, recourse can be made to microphotometric methods for determining the blackening of the image, and hence, from a knowledge of the characteristics of the film used (*i.e.*, the relation between intensity of incident radiation and the blackness produced), the intensities of the diffracted beams calculated. The data so obtained, *i.e.*, interplanar spacings and intensities of diffraction beams, are characteristic of the material examined, and any substance which yields precisely the same data is definitely identified as one and the same material.

The utility of the method therefore depends upon diffraction data of many substances being on record (*e.g.*, "International Critical Tables"; I. E. Knaggs, B. Karlik, and C. F. Elam "Tables of Cubic Crystal Structure," Hilger, 1932) and preferably classified to assist rapid identification. Hanawalt's card catalogue system,¹⁵ in which the three strongest lines are given for over 1,000 substances, greatly facilitates identification.

A striking example of the ability of the diffraction method to give a result where standard chemical methods are impotent is that of the detection of crystalline silica in lung tissue.¹⁶ A chemical attack of this problem would not differentiate between free and combined, crystalline or amorphous silica in the lung, since when differentiation is attempted the silica may react with the alkaline constituents of the ash at the temperature necessary to eliminate carbon. Quartz was detected in tissue containing only 0.26% of silica.

A second example is found in the work on the effect of sodium fluoride and parathormone on the incisors and tibiae of rats,¹⁷ in

¹⁵ J. D. Hanawalt and H. W. Rinn, *Ind. Eng. Chem. (Anal.)*, 1936, **8**, 244; J. D. Hanawalt, H. W. Rinn, and L. K. Frevel, *Ind. Eng. Chem.*, 1938, **30**, 457.

¹⁶ R. Klaas, H. C. Sweany, J. N. Mrgudich, and G. L. Clark, *Science*, 1937, **86**, 544.

¹⁷ L. Reynolds, K. E. Corrigan, H. S. Haydn, I. G. Macy, and H. A. Hunscher, *Amer. J. Roentgenol.*, 1938, **39**, 103.

which X-ray patterns showed that the brittleness of the teeth was due to lack of orientation, increased crystal size, and heterogeneity of the material.

As a positive test the diffraction method is unequivocal, but as a negative test it must be accepted with caution. If the pattern of the substance sought for is obtained, then that substance is present: but the possibility of some other crystalline material of low sensitivity mixed with it, or the presence of some substance in solid solution that has not appreciably altered the lattice cannot be excluded. If no pattern is obtained, an upper limit, which may be high, can be set to the amount present. A pattern different from that expected does not necessarily mean that the material is absent, for traces of impurity in solid solution can change the interplanar spacings. For example, K. N. Ivanov and O. K. Kundra¹⁸ observed that the lattice parameters of copper, cadmium, cuprous oxide, and zinc oxide and the powder-like cathode precipitates obtained from aqueous solution at high current density were increased up to 100% by the absorption of hydrogen. This apparent disadvantage can in some cases be turned to good use, and the extent of solid solubility may be determined by the change in the lattice parameters of the solvent.

Within these limitations, the method can be extended to the identification of mixtures, which requires two or more patterns to be found which give an exact match with that of the unknown material. Once the components are identified, quantitative estimation is possible by comparison of the diffraction pattern of the sample with those of prepared standard mixtures. T. N. Agafona,¹⁹ using a photometric method, determined the variation in the relative intensity ratio of suitable pairs of lines of binary (A-B) mixtures, including apatite-alumina and $\text{MnO}_2\text{-Mn}_2\text{O}_3$, with percentage composition. By adding a known percentage of standard B (*e.g.*, iron, aluminium, or sodium chloride) to a mixture containing an unknown amount of A, and determining the intensity ratios, the amount of A present was read off the intensity ratio-percentage composition curve. In certain cases the error was less than 1%. A similar method in which an added known material served as an internal standard was used by G. L. Clark and D. H. Reynolds²⁰ in the analysis of mine dusts. K. Schäfer,²¹ using a photometric method for the determination of the intensities of selected reflexions from certain 1:1 binary mixtures and alloys, obtained results accurate to 3%.

¹⁸ *J. Phys. Chem. Russia*, 1935, **6**, 469.

¹⁹ *Compt. rend. Acad. Sci. U.R.S.S.*, 1937, **16**, 367.

²⁰ *Ind. Eng. Chem. (Anal.)*, 1936, **8**, 36.

²¹ *Z. Krist.*, 1938, **99**, 142.

Though microscopy and thermal analysis are the usual tools for exploring the composition and structure of phase systems, the diffraction method must now rank with them. To summarise the vast quantity of work of this type is virtually impossible, and the investigations on tin bronzes,²² on the binary systems $\text{TiO}_2\text{-MgO}$, $\text{ZrO}_2\text{-MgO}$, $\text{ZrO}_2\text{-TiO}_2$ and the correlation of information so obtained with the ceramic properties of certain mixtures,²³ the equilibrium diagrams of ternary alloys,²⁴ the Mg-Ca ,²⁵ Au-Hg ,²⁶ Al-Mg ,²⁷ Co-Sn ²⁸ systems are quoted only as examples of recent additions to the subject.

The method has also been extensively used in other fields. The differentiation of the micas,²⁹ the analysis of Estonian blue clay,³⁰ and the presence of cristobalite in glass³¹ illustrate rather than define the catholicity of its powers. X-Ray diffraction has shown that a chemical compound is formed when litharge and titania are calcined in equimolecular proportions.³² The reactions occurring in lead-acid storage batteries, which have been the subject of study for the past 50 years, have been elucidated by evidence in support of the double sulphate theory.³³ Though many examples may be chosen in which X-ray methods have given the necessary and sufficient analyses unaided by other physical or chemical methods, it should be recognised that in their value as an auxiliary weapon—auxiliary as the five senses are auxiliary one to another—lies their general utility in the analytical laboratory. Just as in the analysis of a single material, gravimetric, volumetric, electrolytic, colorimetric, spectrographic, and microscopic methods (to name a few) are frequently used, each cross-checking and supplementing the other, so X-ray methods may dovetail with these to give a clearer answer to analytical problems.

²² T. Isawa, *Mem. Ryojun Coll. Eng.*, 1937, **10**, 53.

²³ W. Büssem, C. Schusterius, and A. Ungewiss, *Ber. deut. keram. Ges.*, 1937, **18**, 433.

²⁴ A. J. Bradley, H. J. Goldschmidt, H. Lipson, and A. Taylor, *Nature*, 1937, **140**, 543.

²⁵ K. Riederer, *Z. Metallk.*, 1937, **29**, 423.

²⁶ I. N. Plaskin, *Ann. Sect. Anal. Phys. Chim.*, 1938, **10**, 129.

²⁷ F. Laves and K. Moeller, *Z. Metallk.*, 1938, **30**, 232.

²⁸ O. Nial, *Z. anorg. Chem.*, 1938, **238**, 287.

²⁹ G. Nagelschmidt, *Z. Krist.*, 1937, **97**, 541.

³⁰ W. Pralow, *Chem. Erde*, 1938, **11**, 480.

³¹ A. A. Lebedev, *Bull. Acad. Sci. U.R.S.S.*, 1937, Ser. Phys., 381; B. E. Warren and J. Biscoe, *J. Amer. Ceramic Soc.*, 1938, **21**, 49.

³² D. G. Nicholson, *Ind. Eng. Chem.*, 1937, **29**, 716.

³³ C. S. Barrett, *ibid.*, 1933, **25**, 297.

3. APPLICATIONS OF ELECTRON DIFFRACTION.

It is little more than ten years ago that L. de Broglie's suggestion that electrons were associated with wave systems was experimentally verified by C. J. Davisson and C. H. Kunsman³⁴ and by G. P. Thomson and A. Reid.³⁵ The wave-length λ corresponding to an electron velocity v is given by the equation

$$\lambda = \frac{h}{mv} \text{ or } \lambda = h \sqrt{\frac{150}{ePm_0}} / \sqrt{1 + \frac{eP}{600m_0c^2}}$$

where h is Planck's constant, P is the potential difference through which electrons are accelerated, e the charge and m_0 the rest mass of the electron. For example, electrons accelerated through a potential difference of 30—70 kv. have an associated wave system of wave-length 0.07—0.05 Å. It is interesting to compare these values with the shortest X-rays regularly used, namely, the K_α radiation of tungsten, which has a wave-length of more than 0.2 Å.

An electron beam on striking a crystalline surface is subjected, just as are X-rays, to diffraction governed by the Bragg equation, and the applicability of electron diffraction to analysis is comparable to that of X-rays, with the difference that the low penetrability of electrons is turned to advantage in the examination of surface films. Whereas X-rays pass through the surface atoms without being much affected and penetrate to great depth, electrons, being charged and easily deflected by the intense fields of the atomic nuclei, are diffracted strongly by the outermost layer. Hence, to be suitable for examination by a transmitted electron beam, films should be not more than a few hundred Å. thick; the same film examined by transmitted X-rays would scatter into the pattern only a negligible proportion of the incident beam. Relatively bulky specimens may be examined by reflexion, the incident electron beam at grazing incidence being used, the half-pattern so produced being characteristic of the crystalline state of the surface layer. X-Rays diffracted in the same manner give a pattern in which the influence of an invisibly thin surface layer is overwhelmed by the effect of the underlying layers. When the bulk sample is of the same composition, structure, grain size, state of strain, and orientation as the outer 10^{-6} inch layer, then this difference will not operate to the disadvantage of the X-ray method, but for the examination of very thin films produced, *e.g.*, by electro-deposition, sputtering, precipitation from colloidal suspension, condensation of vapours, oxidation and other chemical reactions at metal surfaces, the use of the electron beam presents the only method of attack. That exposures

³⁴ *Science*, 1921, **54**, 522.

³⁵ *Nature*, 1927, **119**, 890.

of only fractions of a second are required compared with the hours that are usual in X-ray work is an incidental but not inconsiderable advantage.

It is of primary importance that, in general, the electrons have no effect on the specimen, yet the possibility of a positive influence in exceptional cases cannot be ignored. The fading of the pattern of gold leaf, observed by J. J. Trillat and S. Oketani,³⁶ was not in agreement with the results of G. I. Finch, A. G. Quarrell, and H. Wilman,³⁷ who have suggested that the observed phenomenon was due to condensation on the specimen of metal evaporated from the hot filament used as an electron source. The observation of the decomposition of silver bromide and iodide into their constituent elements³⁸ has not been contraverted. Finch, however, finds that silver chloride is unaffected. Since the diffraction pattern in any case is determined by the surface of the specimen, it is evident that great care must be exercised to exclude all sources of contamination.

The electron-diffraction pattern of platinum sputtered in oxygen showed the presence of an oxide, though the film had all the appearance of platinum,³⁹ and the bloom which formed on silver used as a catalyst for the oxidation of methanol and was suspected of being a compound, was shown to be only the metal.⁴⁰

The composition of certain oxide films and their relation to protection against corrosion has been the subject of investigation by electron diffraction. Recent work in this field includes the observation that iron heated in air at 800–900° gave a film of relatively large crystals of α -ferric oxide in the (100) orientation which has low corrosion resistance,⁴¹ whereas "blued" (nitre) steel has a fairly resistive crystalline surface layer of γ -Fe₂O₃ or Fe₃O₄, the crystals being much smaller.⁴⁰

The film from iron made passive with potassium chromate has been examined by transmitted electrons, and that from iron made passive by nitric acid or potassium chromate by the reflexion method; the protective film was deduced to be γ -Fe₂O₃.⁴² The method has also been used for the study of the grain boundaries in iron,⁴³ and the presence of Fe₃C and either iron or iron oxide at the grain boundaries inferred.

³⁶ *Compt. rend.*, 1936, **202**, 1332.

³⁷ *Trans. Faraday Soc.*, 1935, **31**, 1051.

³⁸ J. J. Trillat and H. Motz, *J. Physique*, 1936, **2**, 89; J. J. Trillat and R. Merigoux, *J. Phys. Radium*, 1936, **7**, 497.

³⁹ G. I. Finch, *Proc. Roy. Soc.*, 1933, **141**, 414.

⁴⁰ *Idem*, unpublished.

⁴¹ G. D. Preston and L. L. Bircumshaw, *Trans. Faraday Soc.*, 1935, **31**, 1051.

⁴² T. Imori, *Bull. Chem. Soc. Japan*, 1938, **13**, 152.

⁴³ R. Morgan, S. Steckler, and B. L. Miller, *J. Chem. Physics*, 1937, **5**, 953.

Gold leaf in oxygen at 450° gives a pattern which disappears on heating at 400° in a vacuum, and has been interpreted as being probably due to the formation of an oxide;⁴⁴ gold foil containing copper, when heated in air, gives a pattern interpretable as being due to the formation of cupric oxide.⁴⁵

4. POLAROGRAPHIC ANALYSIS.

Polarographic methods of analysis, due initially to Heyrovský and his co-workers, were last dealt with in the Reports for 1933, where the opinion was expressed that the method should find wider applications. Further work has elucidated the various physical phenomena encountered, and Heyrovský¹ has compiled an extensive bibliography of the work of his school on the determination of various ions and molecules in solution, both separately and together. It is only during the last two years, however, that the method has found any extended use by other workers, and several recent papers have described successful applications of the method to routine analysis, where the speed with which a number of determinations of exactly the same type can be carried out well repays the time spent in working out the optimum conditions of analysis.

With the technique most generally employed now, a solution of the material to be examined is made the electrolyte of a cell in which the anode is a pool of mercury and the cathode is a dropping-mercury electrode. A potential, slowly increasing from 0 to 2 or 4 volts, is applied to the cell by means of a rotating potentiometer, which is directly geared to a recording drum. A strip of photographic paper is wrapped around the drum, and the current passing through the cell is automatically recorded by means of a beam of light reflected from the mirror of a galvanometer in the circuit. In this way current-voltage curves are recorded for the cell. The electrical resistance of the electrolyte in the cell is made negligible by the addition of a salt such as lithium or tetramethylammonium chloride, in which the cation has a high deposition potential. Since the area of the anode is large relative to that of the dropping electrode, and therefore unpolarisable, the resistance of the whole cell is determined solely by the processes occurring at the cathodic mercury-water interface. As the *E.M.F.* across the cell is raised gradually from zero, the current passed by the dropping electrode remains negligible until the deposition or reduction potential of one of the ions or molecules present in the electrolyte is reached.

⁴⁴ G. L. Clark and E. Wolthus *J. Appl. Physics*, 1937, 630.

⁴⁵ J. J. Trillat, S. Oketani, and S. Miyaké, *J. Phys. Radium*, 1937, 8, 353.

¹ J. Heyrovský and J. Klumpar, *Coll. Czech. Chem. Comm.*, 1938, 10, 153.

At this point a sudden but limited increase in current occurs and concentration polarisation sets in. The cathodic interface becomes denuded of cations with that deposition or reduction potential, and further electrolysis is limited by the rate at which fresh material can diffuse to the interface from the bulk of the solution. Further increase in the applied voltage produces no increase in the diffusion current until the next deposition or reduction potential is reached. Current-voltage curves obtained in this way consist of steps or waves; the voltage at which the wave occurs is a qualitative indication of the material responsible, and the height of the wave is a measure of its concentration.

The apparatus itself has been improved. For instance, by imposing a small *A.C.* voltage on the ordinary *D.C.* voltage applied to the cell, any desired portion of the current-voltage curve can be viewed continuously on a cathode ray oscillograph. No recording is required, and interpretation is similar to that employed in the classical method.² The photographic method of recording has been replaced by a recording pen actuated through an amplifier, whereby advantages in speed and ease of manipulation are obtained.³ Further modification is described in connexion with the determination of copper in blood.⁴

The construction of capillary tubes suitable for the dropping electrode requires care, since the internal and external diameters of the drawn-out tip and other dimensions all influence the dropping time of the electrode and, therefore, the polarograms obtained with it. Dislocation of routine work caused by breakage of a capillary in the middle of a series of analyses may be avoided by the production of standard capillary electrodes from thermometer tubing.⁵ It is claimed that results with these electrodes vary but little from one electrode to another.

The theory underlying the polarographic method has been examined in relation to the diffusion currents (which are the quantitative factor in a polarogram) and their variation in the presence of a large excess of an indifferent electrolyte. D. Ilkovic⁶ has derived the relationship

$$i_D = 0.63nFCD^{\frac{1}{2}}m^{\frac{1}{2}}t^{\frac{1}{2}}$$

where n is the valency of the ion undergoing electrolysis, C its

² R. H. Müller, R. L. Garman, M. E. Droz, and J. Petras, *Ind. Eng. Chem. (Anal.)*, 1938, **10**, 339.

³ H. C. Gull, *J. Soc. Chem. Ind.*, 1937, **56**, 177 π .

⁴ A. Roncato and B. Bassani, *Arch. Sci. biol.*, 1936, **19**, 541; *Chem. Zentr.*, 1938, i, 4772.

⁵ H. Siebert and T. Langer, *Chem. Fabr.*, 1938, **11**, 141.

⁶ *J. Chim. physique*, 1938, **35**, 129.

concentration, D its diffusion coefficient in solution, F Faraday's constant, m the mass of mercury flowing from the dropping electrode per second, and t the drop time in seconds. He has also found the temperature coefficient of the diffusion current to be about 1.63% per degree for most ions.⁷ J. Maas⁸ has confirmed these results experimentally and shown that with cadmium sulphate in 0.1N-potassium chloride the diffusion current varies directly with the concentration of cadmium sulphate unless the dropping time of the capillary is below 3.8 seconds and an unusually high pressure of mercury is employed in the capillary. Under these conditions he has found that the diffusion current tends to increase with increasing applied voltage instead of remaining constant. Other workers have investigated the theoretical aspects of diffusion currents with and without an excess of indifferent electrolyte present,⁹ and also with stationary and with growing mercury drops.¹⁰

Other factors affecting the quantitative aspect of polarography have been investigated. The height of the wave obtained with ferrous sulphate and cadmium acetate varies directly with their concentration, but with zinc, stannous, and nickel chlorides the relationship is not linear. The presence of other ions in the solution also depresses the wave height.¹¹ In this connexion the presence of univalent polymerised ions in one-third basic aluminium acetate solution¹² is noteworthy, since such a solution would give a much smaller wave than would be expected from an equivalent concentration of unpolymerised trivalent aluminium.

The concentration of cyanide ions affects the deposition potential and the wave heights associated with nickel in solutions of potassium nickelocyanide,¹³ and wave heights obtained with solutions of various ions are lessened by the addition of primary alcohols, dioxan, trimethylene glycol, and glycerol, the curves being poorly defined for the more viscous solutions.¹⁴

Since the outline and sharpness of waves vary considerably, some standard method must be adopted to obtain consistent results in measuring wave heights for quantitative work. Heyrovský drew tangents at 45° to the axes, touching the curves at the top and the bottom of the wave. The height of the wave was then

⁷ *Coll. Czech. Chem. Comm.*, 1938, **10**, 249.

⁸ *Ibid.*, p. 42.

⁹ D. MacGillavry and E. K. Rideal, *Rec. Trav. chim.*, 1937, **56**, 1013, 1039.

¹⁰ *Idem, ibid.*, 1938, **57**, 33.

¹¹ P. N. Pavlov, *J. Gen. Chem. Russia*, 1937, **7**, 2246.

¹² C. Rohmann and W. Mirus, *Arch. Pharm.*, 1937, **275**, 541.

¹³ J. P. Gochachtein, *J. Gen. Chem. Russia*, 1937, **7**, 2486.

¹⁴ E. S. Peracchio and V. W. Meloche, *J. Amer. Chem. Soc.*, 1938, **60**, 1770.

taken as the vertical distance between the points of contact. Other procedures are discussed in a paper dealing with the determination of ketones by this method.¹⁵

Large and sharply defined maxima sometimes occur at the top of an ordinary wave in a polarogram. These are generally ascribed to adsorption effects¹⁶ but their appearance is frequently confusing. They may be suppressed by adding colloidal material such as gelatin to the solution, and for the production of clear and distinct polarograms, H. Hohn¹⁷ recommends a series of standard electrolyzing solutions ("Grundlösung") containing colloidal material, complex-forming reagents, and indifferent electrolytes suitable for specific analyses. Certain features of the somewhat similar maxima obtained when nitro-compounds are reduced at the dropping electrode are not explained by existing theory.¹⁸ The maxima vary with p_H , and it is suggested that the accumulation of reduction products at the interface is responsible for the observed phenomena.

When solutions to be analysed contain two or more ions with deposition potentials so close that only one wave results and separation for purposes of measurement is impossible, addition of a reagent to form a complex with one or both of the ions may effect either a shift of the deposition potential or a total suppression of the wave associated with one of the ions. Sometimes adjustment of the p_H will achieve this result. The deposition potentials of nickel and zinc present together in neutral or slightly acid solution are too close for separation. Addition of ammonium acetate and adjustment of the p_H to 8.5 with aqueous ammonia produces a separation of 0.3 volt,¹⁹ and addition of gelatin and ammonia separates them by 0.4 volt.²⁰ In this way two distinct and measurable waves are obtained. Similar methods are adopted when examining plant ash for zinc in the presence of nickel, cobalt, cadmium, lead, copper, and bismuth.²¹

Adaptation of the polarograph has been described for the routine analyses of copper²² or of copper, nickel, and cobalt present

¹⁵ G. T. Borchardt, V. W. Meloche, and H. Adkins, *J. Amer. Chem. Soc.*, 1936, **59**, 2171.

¹⁶ See, e.g., J. Heyrovský and E. Vascutzanu, *Coll. Czech. Chem. Comm.*, 1931, **3**, 418; N. V. Emelianova and J. Heyrovský, *Trans. Faraday Soc.*, 1928, **24**, 257.

¹⁷ "Chemische Analysen mit dem Polarographen," Julius Springer, Berlin, 1937, pp. 41—44.

¹⁸ A. Winkel and H. Siebert, *Z. Elektrochem.*, 1938, **44**, 402.

¹⁹ P. R. Stout and J. Levy, *Coll. Czech. Chem. Comm.*, 1938, **10**, 136.

²⁰ P. N. Pavlov and G. S. Pavlenko, *J. Gen. Chem. Russia*, 1937, **7**, 2259.

²¹ P. R. Stout, J. Levy, and L. C. Williams, *Coll. Czech. Chem. Comm.*, 1938, **10**, 129.

²² J. I. Usatenko and J. S. Lialikov, *Zavod. Lab.*, 1937, **6**, 1394.

together²³ in steel, and of aluminium, manganese, zinc, and lead within certain limits of concentration in magnesium alloys.²⁴ The limitations of the method when applied to the analysis of brasses have been examined,²⁵ and the polarograph has been found satisfactory for the determination of the total alkali metals, after removal of calcium and magnesium, in mineral waters and natural plant ashes where the concentration is of the order of 0.001N.²⁶ The determination of traces ($>0.00001\%$) of lead and arsenic in reagent phosphoric acid presents some unusual features.²⁷ The two ions, present together, are determined in the presence of concentrated phosphoric acid with the addition of hydrochloric acid after reduction of quinque- to ter-valent arsenic by boiling with hydrazine.

An examination of the behaviour of aconitic acid undergoing reduction at the interface of the dropping electrode²⁸ has led to a method for the analysis of mixtures of the *cis*- and the *trans*-acid.²⁹ The behaviour of quinoline and quinine³⁰ and of camphor and bilirubin³¹ has also been examined. General applications of the method to inorganic, organic, and microanalysis have been discussed by A. Winkel and G. Proske.³²

In the biological sphere, the polarograph has found several applications by reason of the small quantities of material that can be examined successfully. The determination of lead in blood requires but 2 c.c. of material,³³ and a method for copper in blood is also given.³⁴ Vitamin-C may be determined in the absence of air in concentrations as low as $10^{-5}M$,³⁵ and 1 $\mu g.$ in 1 c.c. of water can be detected. Constituents other than vitamin-C, present in extracts from animal tissues, hinder the electrode reaction.

No summary of progress in polarographic analysis would be complete without reference to the work of R. Brdicka on the determination of proteins especially in regard to the detection of carcinoma, of which a summary has been given recently by Heyrovský.³⁶ Addition of protein to a solution containing

²³ *Angew. Chem.*, 1937, **21**, 375.

²⁴ H. C. Gull, *loc. cit.*, ref. (3).

²⁵ E. Mnich, *Z. Elektrochem.*, 1938, **44**, 132.

²⁶ N. V. Komar, *Zavod. Lab.*, 1937, **6**, 1074.

²⁷ T. A. Kriukova, *ibid.*, p. 1385.

²⁸ G. Semerano and G. Bettinelli, *Mem. R. Accad. Ital.*, 1937, **8**, 243, 255.

²⁹ G. Semerano and L. Sartori, *Mikrochem.*, 1938, **24**, 130.

³⁰ I. Tachi and H. Kabai, *J. Electrochem. Assoc. Japan*, 1935, **3**, 250.

³¹ I. Tachi, *Mem. Coll. Agric. Kyoto*, 1938, No. 42, 2.

³² *Angew. Chem.*, 1937, **50**, 18—25.

³³ J. Teisinger, *Z. ges. exp. Med.*, 1936, **98**, 520.

³⁴ A. Roncato and B. Bassani, *loc. cit.*, ref. (4).

³⁵ E. Kodíček and K. Wenig, *Nature*, 1938, **142**, 35.

³⁶ *Ibid.*, p. 317; see also O. M. Henriques and C. G. Wolffbrandt, *ibid.*, p. 212; and E. C. Dodds, *Lancet*, 1938, **235**, 351.

ammonium and cobalt salts gives a polarogram having a series of maxima between 0.8 and 1.8 volts.³⁷ These correspond to the evolution of hydrogen, which occurs at a lower overpotential in the presence of protein. The effect of the protein is catalytic, and is associated with the presence of thiol radicals, the activity of which is decreased by the incidence of carcinoma. Protein derived from carcinomatic sera, therefore, gives lower maxima. An alternative method involves a somewhat similar determination of the albuminose content of the serum which, in cases of carcinoma and also in certain cases of fever or inflammation, is unusually high. The determinations can be carried out on as little as 0.2 c.c. of blood.

5. APPLICATIONS OF RAMAN AND ABSORPTION SPECTRA.

Light incident on a molecule suffers one of several fates, depending upon its wave-length and the nature of the molecule: it may be transmitted, scattered, or absorbed.

Raman Spectra.—Of the incident light scattered, a small proportion may be found differing in wave-lengths from the incident light. These changes of wave-length, or frequency, produced by scattering, constitute the Raman effect.¹ In general, each different linkage and structure has characteristic Raman frequencies, which may be modified slightly by the rest of the molecule, but are generally unaffected by the presence of foreign molecules. In principle, therefore, the Raman spectrum may be used to identify a compound in terms of its structure, and to determine the proportion present in a mixture, since the intensity of each line is proportional to the concentration of the entity concerned. The dust-free sample (solid, liquid, or gas) is irradiated by means of strong monochromatic light, usually from a mercury arc, and the spectrum of the scattered light is recorded by exposing a photographic plate for several hours in a wide-aperture spectrograph. Alternatively, the intensity of the lines may be determined by replacing the plate with a second slit and a photoelectric counter.² Any fluorescence of the sample is minimised, *e.g.*, by adding an inhibitor such as nitrobenzene.³ The Raman-spectrum method is especially valuable in the analysis of unstable substances in equilibria which cannot be "frozen," as in the identification and determination dinitrogen pentoxide in nitric-sulphuric acid mixtures.⁴ The method has succeeded with mixtures of very similar and difficulty separable substances.

³⁷ R. Brdicka, *J. Chim. physique*, 1938, **35**, 89.

¹ *Ann. Reports*, 1934, **31**, 22.

² V. Kudrjavzeva, *Acta Physicochim. U.R.S.S.*, 1935, **3**, 613.

³ J. H. Hibben, *Ind. Eng. Chem.*, 1934, **26**, 646.

⁴ J. Chédin, *Ann. Chim.*, 1937, [xi], **8**, 243.

Hydrolysates from proteins containing a limited number of amino-acids can be analysed, but with more complex mixtures, serious overlap of the lines interferes.⁵ Valuable results have been obtained in identifying the constituents of essential oils and products from terpenes,⁶ and simple mixtures of similar hydrocarbons have been analysed by several authors. J. Goubeau⁷ has analysed mixtures of benzene, toluene, and the xylenes by measuring the persistence of the Raman lines through a series of standardised exposures decreasing in geometrical progression, and comparing them with the intensities derived from the pure substances, but quantitative results are unreliable with lines of low intensity. L. Piaux⁸ identified Δ^{α} -pentene and *cis*- and *trans*- Δ^{β} -pentene in the dehydration product of β -pentanol by means of small specific differences between the ethylenic frequencies.

Absorption Spectra.—In general terms, radiations absorbed in the far infra-red part of the spectrum correspond with changes in the rotational energy of the absorbing molecules, those absorbed in the near infra-red correspond with changes in the vibration and rotation, and those absorbed in the visible and ultra-violet correspond with electronic transitions accompanied by vibrational and rotational changes. In recent years, electronic absorption spectra have received extensive analytical applications, as in vitamin investigations, and it is now apparent that infra-red absorption spectroscopy has its own largely undeveloped field of utility.

(i) *Infra-red absorption spectra.* These can be used to identify a substance by observing exact coincidences of a large number of bands in the unknown with those in the absorption spectrum of a given compound. Thus, a large proportion of methane has been found in the atmospheres of the major planets by means of photographs of the absorption spectra at wave-lengths less than $1\ \mu$.⁹ Radiation of wave-length greater than about $1.2\ \mu$ is determined by a thermopile-galvanometer system, and with the increase in resolving power and precision of infra-red spectrometers,¹⁰ the recognition that absorption bands near certain wave-lengths are due to the vibrations of particular groupings of atoms renders it possible to identify substances in terms of the actual wave-lengths and character of the absorption bands and to determine the proportions of the ingredients in mixtures. For example, the concentrations of

⁵ N. Wright and W. C. Lee, *Nature*, 1937, **139**, 551.

⁶ *E.g.*, G. Dupont, V. Desreux, and R. Dulou, *Bull. Soc. chim.*, 1937, [v], **4**, 2016.

⁷ *Z. anal. Chem.*, 1936, **105**, 161.

⁸ *Chim. et Ind.*, 1935, **34**, 507.

⁹ A. Adel and V. M. Slipher, *Physical Rev.*, 1934, [ii], **46**, 902.

¹⁰ *E.g.*, J. J. Fox and A. E. Martin, *Proc. Roy. Soc.*, 1937, *A*, **162**, 419.

imino-, amino-, and hydroxy-groups in carbon tetrachloride solutions of organic substances were determined by absorption observations in the region $1.65\text{--}1.35\ \mu$,¹¹ and constituents of petroleum fractions were identified by means of their absorption spectra in the range $7\text{--}20\ \mu$.¹² Absorption maxima due to a particular group in molecules, very similar chemically, may differ in character and wave-length, and such differences, although small, can be utilised analytically; for instance, traces of 2- and 4-hydroxydiphenyl were identified and determined in samples of synthetic phenol by removing the phenol in a vacuum and using the observation that, in carbon tetrachloride, 2-hydroxydiphenyl has a double hydroxyl absorption band of which the weaker limb is at $2.77\ \mu$, whereas phenol and 3- and 4-hydroxydiphenyl have a single sharp band at $2.77\ \mu$. Bands near $3.27\ \mu$ due to CH are affected by small changes in the molecule, and phenol and 4-hydroxydiphenyl have sharp absorption peaks at $3.283\ \mu$ and $3.295\ \mu$, respectively, easily distinguished from the less prominent, corresponding, peaks of 2- and 3-hydroxydiphenyl.¹³

(ii) *Visible and ultra-violet absorption spectra.* In little more than a decade, colorimetric and absorption spectrometric methods have been developed extensively for detecting and determining small quantities of substances which cannot be isolated conveniently or quantitatively. The recent Report on colorimetry¹⁴ includes topics germane to absorption spectrophotometry also, and these matters will not be detailed here. Few tests in chemistry are "specific" in the sense recently defined,¹⁵ but inasmuch as colours, different spectroscopically, may be indistinguishable visually, so is the spectrometric method more "selective" than the colorimetric. However, an absorption band with a maximum at a particular wave-length is not necessarily proof of the presence of a particular substance, but it may be characteristic of a particular group of atoms in the molecule. For instance, each of the ergot alkaloids has a maximum at $318\text{ m}\mu$ and a minimum at $270\text{ m}\mu$,¹⁶ and the therapeutically more important ergometrine can be distinguished from ergotoxine and ergotamine since these, unlike ergometrine, do not develop a transient absorption maximum at $289\text{ m}\mu$ during photo-decomposition.¹⁷

Providing Beer's law is obeyed, *i.e.*, the light absorbed at wave-length λ by a substance is proportional to its concentration C , the

¹¹ O. R. Wulf and U. Liddel, *J. Amer. Chem. Soc.*, 1935, **57**, 1464.

¹² P. Lambert and J. Lecomte, *Compt. rend.*, 1938, **206**, 1174.

¹³ Journal, Brit. Ass., 1938, p. 26, and unpublished work.

¹⁴ *Ann. Reports*, 1936, **33**, 456.

¹⁵ *Ibid.*, 1937, **34**, 489.

¹⁶ S. Smith and G. M. Timmis, *J.*, 1937, 396.

¹⁷ I. Bennekou and S. A. Schou, *Dansk Tidsskr. Farm.*, 1936, **10**, 105.

absorption density is related to the thickness l of the homogeneous medium and the molecular extinction coefficient ϵ_λ by

$$\log I_0/I = \text{absorption density} = \epsilon_\lambda Cl$$

where I_0 is the intensity of the incident and I that of the transmitted light. It follows that the accuracy of absorption-density measurements controls that of the concentration deduced. It is important to remember that the above relationship applies strictly only for monochromatic light, although it is near the truth for a region of absorption in which ϵ changes little with wave-length. For determining a substance, such as benzene, from the absorption density at a wave-length corresponding with a sharp absorption peak, observations with light of a single wave-length alone afford trustworthy results.¹⁸

Technique has been advanced, in particular by replacing the eye as a colour or density matching instrument by photo-cell arrangements, thereby increasing accuracy and rapidity of observation. The fraction of incident monochromatised light transmitted by the homogeneous medium may be determined photoelectrically. For example, gaseous chlorine can be determined by using 365 m μ mercury light,¹⁹ or if there is no such convenient source of appropriate monochromatic light, spectrally continuous light and a monochromator may be employed. A recent photoelectric spectrophotometer provides and uses bands only 1—11 Å. broad at any wave-length between 2200 and 7000 Å.,¹⁸ and such an instrument can also be employed for determining the absorption curve of a substance to be characterised by its spectrum. A self-recording instrument²⁰ has been used for investigating optimum conditions for colorimetric determinations.²¹ In other methods, spectroscopically undispersed light is incident on the medium, and the portion transmitted is spectrally resolved and either determined photometrically, *e.g.*, in the visible by matching with a similar part of the "unabsorbed" light beam which is diminished to a determinable extent,²² or recorded photographically, the blackening of the plate at a point corresponding with a particular wave-length being a measure of that light transmitted. The general contour of the ϵ - λ relationship, *i.e.*, the absorption spectrum, is obtained by using

¹⁸ T. R. Hogness, F. P. Zscheile, and A. E. Sidwell, junr., *J. Physical Chem.*, 1937, **41**, 379.

¹⁹ M. Ritchie and R. G. W. Norrish, *Proc. Roy. Soc.*, 1933, *A*, **140**, 99.

²⁰ J. L. Michaelson and H. A. Liebhafsky, *Gen. Electric Rev.*, 1936, **39**, 445.

²¹ J. P. Mehlig, *Ind. Eng. Chem. (Anal.)*, 1938, **30**, 136.

²² As, *e.g.*, in the Hilger-Nutting spectrophotometer (for improvements, see J. H. Dowell, *J. Sci. Instr.*, 1931, **8**, 382).

an arc source emitting very many spectral lines and observing on the plate the wave-length of points of equal density in pairs of spectra, one from the solution under investigation and the other from the solvent, the density from the latter having been reduced in a known ratio.²³ Sufficient spectra can now be photographed simultaneously with a notched echelon cell, thereby minimising any effects of changing absorption or photo-decomposition.²⁴

When *details* of an absorption spectrum are required, a spectrally-continuous source, such as a hydrogen lamp for the ultra-violet and a filament lamp for the visible, is used, and in a quantitative method, one photographic exposure suffices for the solution, and the solvent is then submitted to a series of exposures of predetermined decreasing duration, thereby providing on the derived microphotographic record of the absorption spectrum a series of standard absorption densities.²⁵ As illustrative of progress in the application of these methods, traces of strongly absorbing substances can be detected and determined in media optically transparent in the appropriate spectral region; *e.g.*, as little as 0.1 mg. of benzene extracted by 10 ml. of alcohol from air or viscera can be identified by means of four sharp absorption bands with maxima at characteristic wave-lengths.²⁶ The concentrations of two substances, with overlapping known absorption spectra, can generally be determined by absorption-density measurements at only two wave-lengths. In this way, tyrosine and tryptophan can be determined in as little as 5 mg. of protein.²⁷ This principle has been extended to the analysis of ternary and quaternary mixtures of carotenoid and chlorophyll pigments.²⁸

In spectrophotometric analysis, possible effects of temperature and solvent on the wave-length of the absorption maximum and the molecular extinction coefficient cannot be ignored, and it is important to eliminate or allow for irrelevant absorption. On the other hand, sources of error can be detected by comparing, spectrophotometrically, absorption and colorimetric results obtained from the same substance. Some of these points are illustrated in recent determinations of vitamin A.²⁹

²³ F. Twyman and C. B. Allsopp give details on this and other topics in "Absorption Spectrophotometry," Hilger, 1934.

²⁴ F. Twyman, *Proc. Physical Soc.*, 1933, **45**, 1.

²⁵ H. C. Gull and A. E. Martin, *J. Sci. Instr.*, 1935, **12**, 379.

²⁶ P. Laurin, *J. Pharm. Chim.*, 1938, **27**, 561.

²⁷ E. R. Holiday, *Biochem. J.*, 1936, **30**, 1795.

²⁸ E. S. Miller, *Cereal Chem.*, 1938, **15**, 310.

²⁹ R. A. Morton, "Practical Aspects of Absorption Spectrophotometry," Institute of Chemistry, 1938; A. E. Gillam and M. S. El Ridi, *Biochem. J.*, 1938, **32**, 820.

6. VITAMINS.

When correlation between a chemical or physicochemical property of a material and its vitamin activity is well established, the chemical methods devised generally have advantages of speed, accuracy, and cheapness when compared with biological assays.¹

(i) Vitamin A in marine fish-liver oil, for example, affords a transient blue colour when antimony trichloride is added to a chloroformic solution of the oil or its unsaponifiable fraction. The colour corresponds with absorption bands having maxima at 620 m μ and 583 m μ , but these are at 603 m μ and 572 m μ in oils of low potency. The maximum at 603 m μ and the blue colour are frequently not fully developed owing to inhibitory substances, but small quantities of bromine in the reagent result in greater absorption at 603 m μ and in ratios of E_{603}/E_{572} approaching the corresponding value for the pure vitamin.² Personal errors are eliminated by means of a photo-electric colorimeter, and the contribution to the blue colour by any carotene present is determined by measuring the absorption of the original solution at 440 m μ and multiplying by the appropriate factor derived from experiments with pure carotene.³

The unsaponifiable fraction of fresh-water fish-liver oils gives a green colour, owing to the presence of a factor (or vitamin) A₂ which affords a maximum absorption at 693 m μ . The ratio of the absorptions at 620 and 693 m μ does not, however, correspond with the ratio of vitamins A₁ and A₂, since the latter affords some absorption at 620 m μ .⁴ Oils containing vitamin A, in chloroform, give with perchloric acid, guaiacol, and phenol, a violet colour changing to bright red, which appears to be specific for the vitamin, and is not given by inactive carotene.⁵

Vitamin A in alcoholic solutions has a broad absorption band in the ultra-violet with a maximum at 328 m μ . In the case of oils of low potency, substances other than the vitamin contribute markedly to the gross absorption; hence the unsaponifiable fraction of the oil is employed for the measurement, and allowance is made for any carotene present, as in butter, by means of absorption measurements at 455 m μ . Oils with high content of vitamin A₂ afford absorption maxima at 280 and 350 m μ instead of 328 m μ .⁶ The decrease of absorption at 325 m μ produced by irradiating an alcoholic

¹ R. A. Morton, "Absorption Spectra of Vitamins and Hormones," Hilger, 1935, describes absorption spectra methods as late as 1934.

² O. Notevarp and H. W. Weedon, *Biochem. J.*, 1938, **32**, 1054.

³ W. J. Dann and K. A. Evelyn, *ibid.*, p. 1008.

⁴ E. Lederer and F. H. Rathmann, *ibid.*, p. 1252.

⁵ A. E. Pacini and M. H. Taras, *J. Amer. Pharm. Assoc.*, 1937, **26**, 721.

⁶ A. E. Gillam, *Biochem. J.*, 1938, **32**, 1496.

solution of a marine fish-liver oil with mercury light of 365 m μ , which destroys vitamin A, is said to be an accurate measure of the vitamin.⁷

(ii) In addition to investigations of the methods of analysis for vitamin B₁ (aneurin) reported last year,⁸ the sensitivity of the formaldehyde-azo-reaction has been increased.⁹ 2:4-Dichlorobenzenediazonium chloride affords a colorimetric determination, other coupled compounds being easily separable.¹⁰

(iii) Nicotinic acid and amide act as anti-pellagra vitamins, and colorimetric determinations of these substances, in the absence of other pyridine derivatives, are based on: (1) the red colour produced when the product of gentle fusion with 1-chloro-2:4-dinitrobenzene is made alkaline,¹¹ and (2) the yellow colour produced by rupturing the pyridine ring with cyanogen bromide and treating the product with an aromatic amine.¹²

(iv) Vitamin C (ascorbic acid) is determined by means of reactions based chiefly on its reducing properties, but it exists in some materials partly as a complex with proteins from which it is released, before determination, by hydrolysis with hydrochloric acid.¹³ The acid in extracts may be partly in a reversibly oxidised state and is reduced by preliminary treatment with hydrogen sulphide. A very selective determination of (reduced) ascorbic acid depends on the reduction of methylene-blue by the acid in the presence of light. By careful control of p_H and light intensity, 0.0045 mg. of ascorbic acid in sodium citrate-bicarbonate buffer, containing thiosulphate to prevent oxidation of the leuco-dye, can be determined titrimetrically.¹⁴ In the absence of buffer at p_H 2, 0.02 mg. of ascorbic per 100 g. may be estimated in deproteinised serum by determining photometrically the residual unreduced dye.¹⁵ In the titration of ascorbic acid with 2:6-dichlorophenol-indophenol, it is said that adventitious oxidation is avoided by extracting vegetable matter with 5—15% sulphuric acid in place of acetic or trichloroacetic acids, thereby eliminating the preliminary hydrogen sulphide treatment. The inactivating effect of any copper is avoided by adding metaphosphoric acid.¹⁶ The method has been adapted so that 1 mg. of the

⁷ A. Chevallier, *Z. Vitaminforschung*, 1938, **7**, 10.

⁸ *Ann. Reports*, 1937, **34**, 401.

⁹ H. W. Kinnersley and R. A. Peters, *Biochem. J.*, 1938, **32**, 1516.

¹⁰ H. Willstaedt and F. Bárány, *Enzymologia*, 1938, **2**, 316.

¹¹ P. Karrer and H. Keller, *Helv. Chim. Acta*, 1938, **21**, 1170.

¹² H. Kringstad and T. Naess, *Naturwiss.*, 1938, **26**, 709.

¹³ E. J. Reedman and E. W. McHenry, *Biochem. J.*, 1938, **32**, 85.

¹⁴ A. A. Policard, M. Ferrand, and E. Arnold, *Bull. Soc. Chim. biol.*, 1938, **20**, 165.

¹⁵ H. Wahren, *Klin. Woch.*, 1937, **16**, 1496.

¹⁶ G. L. Mack and D. K. Tressler, *J. Biol. Chem.*, 1937, **118**, 735.

vitamin per 100 g. of plasma is determined in 0.1 ml. by observing with a photo-electric colorimeter the decrease in concentration of the dye. The p_H is carefully controlled, and cysteine and glutathione then have negligible effect.¹⁷ Ascorbic acid extracted from tissue by aqueous metaphosphoric acid reduces phosphotungstic acid at p_H 3, and the colour produced is measured photometrically. Other reducing substances are inactivated by iodoacetic acid, and the selectivity is greater than that of other methods.¹⁸ Other reactions have been proposed. For instance, as little as 0.0001 mg. of ascorbic acid gives a lilac colour with hydrochloric acid and cacothelin.¹⁹ The reduction by vitamin C of potassium ferricyanide to ferrocyanide, which gives a red-brown colour or precipitate with an ammonium molybdate reagent, is the basis of a very selective colorimetric determination and a "spot" test by which 0.5 μ g. of ascorbic acid in 5 c.mm. can be detected.²⁰ Ascorbic acid reduces, non-reversibly, diazotised sulphanilamide in acid media, and the excess of diazonium ion is determined colorimetrically by coupling with dimethyl- α -naphthylamine.²¹

(v) Vitamin D_2 and D_3 are colorimetrically determined in the absence of tachysterol and large amounts of other sterols or vitamin A by means of the orange colour reaction (maximum absorption at 500 $m\mu$) with antimony trichloride in chloroform.²² Measurements at the absorption maximum (265 $m\mu$) of the vitamins are employed in the specification of these substances, but at present, there appear to be no satisfactory alternatives to biological assays.²³

(vi) Vitamin E (tocopherols), the antisterility factor, is in the unsaponifiable fraction of the benzene extract of the natural material, and is titrated potentiometrically in 80% ethyl alcohol with auric chloride, but carotenoids interfere. The tocopherols have different biological activities and may occur in different ratios in different materials, so only approximate correlation between the titration and the biological activity may be expected.²⁴ α -Tocopherol reduces ferric chloride, and the ferrous iron produced by 0.01–0.4 mg. of tocopherol is determined colorimetrically as the ferrous $\alpha\alpha'$ -dipyridyl complex.²⁵

¹⁷ R. L. Mindlin and A. M. Butler, *J. Biol. Chem.*, 1938, **122**, 673.

¹⁸ A. Fujita and T. Ebihara, *Biochem. Z.*, 1937, **290**, 182.

¹⁹ L. Rosenthaler, *Z. Vitaminforschung*, 1938, **7**, 126.

²⁰ K. V. Giri, *Mikrochem.*, 1937—8, **23**, 283.

²¹ J. V. Seudi and H. D. Ratish, *Ind. Eng. Chem. (Anal.)*, 1938, **10**, 420.

²² H. Brockmann and Y. H. Chen, *Z. physiol. Chem.*, 1936, **241**, 129.

²³ Cf. R. A. Morton, *ibid.*, p. 12.

²⁴ P. Karrer and H. Keller, *Helv. Chim. Acta*, 1938, **21**, 1161.

²⁵ V. Emmerie and C. Engel, *Nature*, 1938, **142**, 873.

7. ALKALOIDS AND OTHER DRUGS.

The importance of drugs in medicine and forensic work is reflected in advances in methods of isolation, identification, and determination, particularly in biological material. Methods of separating drugs from animal matter have generally been based on the Stas-Otto process (1856). This consisted essentially in extracting the active principles with a dilute aqueous alcoholic solution of a weak organic acid and evaporating the filtered extract to low bulk. Proteins, etc., were precipitated and eliminated by a succession of extractions and evaporations with absolute alcohol. The drugs were finally extracted from aqueous solution by immiscible solvents. C. G. Daubney and L. C. Nickolls¹ showed that only 40% of the morphine and quinine injected into rats is recovered by this rather tedious process owing to inefficient extraction and inevitable losses. They obtained good and rapid recovery of six alkaloids by mincing the animal matter while frozen solid, which facilitates fine comminution and cell rupture, and precipitated the protein by warm dilute acetic acid and saturated ammonium sulphate. The alkaloids were then easily extracted from the protein by acidified water, and were recovered by immiscible solvents from the combined acid extracts.

C. P. Stewart, S. K. Chatterji, and S. Smith² treated the minced viscera with 10% trichloroacetic acid, adsorbed the alkaloids from the protein- and fat-free filtrate on kaolin, then adsorbed any veronal on charcoal, and subsequently eluted the alkaloids with hot chloroform, and the veronal with ether. F. Bamford³ claims success with a modified Stas-Otto process in which the protein is precipitated with *acid* or *basic* lead acetate according as alkaloids or barbituric acid derivatives are sought.

(i) Cocaine, extracted from preparations in the usual manner by means of ammonia and immiscible solvents, is usually contaminated with any other bases present; but, utilising the observation that cocaine is extracted by light petroleum from aqueous solutions of its salts in presence of sodium bicarbonate, while many other bases are not, J. R. Nicholls⁴ has isolated and determined cocaine in coca leaves and mixtures with synthetic local anæsthetics and other alkaloids, traces of the latter being destroyed by oxidation with acid potassium permanganate, which does not oxidise cocaine under the conditions employed.

(ii) Ecgonine, the alkaloid to which cocaine is easily hydrolysed, is neither extractable from water by immiscible solvents nor easily identified, but gives with platinic chloride and saturated sodium

¹ *Analyst*, 1937, **62**, 851; 1938, **63**, 560.

² *Brit. Med. J.*, 1937, **790**.

³ *Analyst*, 1938, **63**, 645.

⁴ *Ibid.*, 1936, **61**, 155.

iodide a characteristic microcrystalline precipitate distinguishable from that afforded by betaine.⁵

(iii) The flow of fresh colour reactions for morphine and related alkaloids continues, and W. Deckert⁶ has described a nephelometric determination of morphine, dilauidide, and heroin based on the observation that, of a large number of alkaloids, these have a much lower solubility in vanadomolybdic acid than in molybdic acid. Although there are accurate methods for determining morphine in pure salts, such as by forming an insoluble ether with 1-chloro-2 : 4-dinitrobenzene,⁷ determination of morphine in opium has not been unequivocal owing to the presence of similarly reacting phenolic alkaloids.⁸ R. Eder and E. Wackerlin⁹ review this century-old problem and claim to have solved it by elaborating the classical extraction with calcium hydroxide and re-extraction with immiscible solvents, so that the morphine is completely extracted and the uncertainty of the correction for that remaining in the mother-liquors after precipitation is abolished.

(iv) Ouabain, a glycoside and probable active ingredient of certain arrow poisons, warmed with naphtharesorcinol and concentrated hydrochloric acid, and diluted, gives an amyl-alcoholic extract which, unlike that of strophanthin, has a green fluorescence. Ouabain and strophanthin are determined colorimetrically by the red colour produced with *o*-nitrobenzaldehyde and sodium hydroxide.¹⁰

(v) Malonylurea (barbituric acid) derivatives have been identified hitherto chiefly by m. p. determinations of the drugs and derivatives, and observations of the microcrystalline form. The blue complexes formed with cobalt salts in alkaline organic solution have been extensively investigated. Thus, with aqueous cobalt nitrate-calcium chloride, the barbiturate in methyl alcohol gives a blue precipitate from which the drug is liberated by dilute acid and extracted with ether for identification.¹¹ The colour is due to one or two, but not more, imino-groups, and that due to one such group is stable only in a narrow p_H range.¹² 0.05 G. of a barbiturate in chloroform is determined colorimetrically by means of cobalt acetate and lithium hydroxide in absolute methyl alcohol.¹³ Of

⁵ F. Amelink, *Pharm. Weekblad*, 1938, **75**, 861.

⁶ *Z. anal. Chem.*, 1938, **112**, 241.

⁷ C. Mannich, K. Handke, and G. Baumgarten, *Arch. Pharm.*, 1935, **273**, 97.

⁸ J. R. Nicholls, *Analyst*, 1937, **62**, 440.

⁹ *Quart. J. Pharm.*, 1937, **10**, 680.

¹⁰ W. D. Raymond, *Analyst*, 1938, **63**, 478.

¹¹ M. Pesetz, *J. Pharm. Chim.*, 1938, **28**, 69.

¹² F. L. Kozelka and H. J. Tatum, *J. Pharm. Exp. Ther.*, 1937, **59**, 54.

¹³ H. Oettel, *Arch. Pharm.*, 1936, **274**, 1.

chloroform-soluble substances, only theobromine, theophylline, thymine, and lecithin interfere,¹⁴ and some of these can be separated, and so can certain acids, since alkali barbiturates are decomposed by carbonic acid to give crystalline acids when extracted by ether.¹⁵ Sulphuric acid and formaldehyde give with allyl derivatives a yellow colour and green fluorescence, and with certain phenyl derivatives an intense red. 0.1 Mg. of diallylbarbituric acid ("Dial") gives a specific reaction with a salicylaldehyde reagent. Phenyl derivatives give colours when the products of nitration are treated with acetone.¹⁶ Ten barbiturates have been identified by the different precipitation reactions given with a special Millon's reagent (mercurous-mercuric nitrate).¹⁷

(vi) Sulphanilamide is determined colorimetrically by diazotising the amino-group and coupling the product with dimethyl- α -naphthylamine; 1 part in 20 million parts of water can be detected.¹⁸ Microcrystalline tests have been described.¹⁹

8. CARBOHYDRATES.

The reducing properties of carbohydrates are the basis of most reaction methods of determining these substances. The methods are largely empirical, and progress includes new and improved methods and, in particular, their application to mixtures.

Pentoses.—Interest in the pentose content of plant tissues has led to improvements of the classical distillation of pentoses with hydrochloric acid and determination of the evolved furfuraldehyde as the phloroglucinol derivative. The relation between the latter and furfuraldehyde-yielding substances singly and in admixture has been determined, together with the effects of hexoses,¹ and, as is not infrequent in analysing carbohydrate mixtures, the sum of the yields from single ingredients differs from the yield from the mixture, and therefore corrections are applied. Inconsistencies attributed to the classical method are due to departures from the prescribed technique, and added salt is essential to stabilise the acidity when converting methyl pentoses into methylfurfuraldehyde, which may be precipitated with either phloroglucinol or thiobarbituric acid.²

¹⁴ T. Koppanyi, J. M. Dille, W. S. Murphy, and S. Krop, *J. Amer. Pharm. Assoc.*, 1934, **23**, 1074.

¹⁵ E. Schulek and P. Rozsa, *Z. anal. Chem.*, 1938, **112**, 404.

¹⁶ M. Pesez, *J. Pharm. Chim.*, 1938, [viii], **27**, 247.

¹⁷ M. Paget and F. Tilly, *ibid.*, 1937, [viii], **25**, 222.

¹⁸ *E.g.*, E. K. Marshall, junr., *J. Biol. Chem.*, 1938, **122**, 263.

¹⁹ *E.g.*, F. Amelink, *Pharm. Weekblad*, 1938, **75**, 851.

¹ S. Angell, F. W. Norris, and C. E. Resch, *Biochem. J.*, 1936, **30**, 2146.

² C. R. Marshall and F. W. Norris, *ibid.*, 1937, **31**, 1053, 1939.

Hexoses and Disaccharides.—In sugar analysis, trustworthy determinations of total reducing sugars are of value, and a modified Pellet's solution, consisting of a 1 : 4 mixture of (343.5 g. of $\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$ + 34.35 g. of NH_4Cl per l.) and (216.25 g. of Rochelle salt + 283.5 g. of Na_2CO_3 per l.), determines glucose, fructose, maltose, and lactose and their mixtures and, unlike Fehling's solution, without any interference by sucrose except in the case of lactose mixed with much sucrose.³ A new, but empirical, gravimetric determination of fructose and sucrose alone and in sugar mixtures is based on the fact that they reduce selenious acid to selenium in hot sulphuric acid solutions whereas glucose, galactose, lactose, and maltose have only slight effects.⁴ Reducing sugars convert alkaline potassium ferricyanide into ferrocyanide, and glucose is determined by titrating the ferrocyanide with potassium dichromate in acid solution with diphenylamine as indicator,⁵ or the change in ferricyanide concentration is determined by the ferri-ferrocyanide electrode.⁶

Advances continue to be made in the complete analysis of sugar mixtures. In binary mixtures, glucose is determined by oxidation with sodium hypiodite, and fructose is subsequently determined by a micro-copper-iodide method.⁷ In a method of the latter type, sodium sulphate prevents atmospheric oxidation of the precipitated cuprous oxide,⁸ which is determined iodometrically, thereby permitting 0.01 mg. of glucose to be determined accurately, and imparting to copper reagents the advantages of the (less selective) potassium ferricyanide reagents. The selective destruction of carbohydrates by five micro-organisms, and acid hydrolysis at appropriate stages, together with determinations of reducing values before and after each stage, permit glucose, fructose, mannose, galactose, sucrose, maltose, and lactose to be determined in mixtures of these sugars.⁹

Distinction is made between ketoses, aldoses, and corresponding alcohols by oxidation with potassium periodate, since one mol. of ketose with n carbon atoms consumes $n - 2$ mols. of periodate compared with $n - 1$ mols. by aldoses and alcohols. Oxidation of 1 mol. of alcohol or ketose yields 2 mols. of formaldehyde and $n - 2$ mols. of formic acid compared with 1 mol. of formaldehyde and $n - 1$ mols. of formic acid from 1 mol. of aldose.¹⁰

³ C. Y. Chang and H. A. Shuette, *Trans. Wisconsin Acad. Sci.*, 1935, **29**, 381.

⁴ G. Reif, *Z. Unters. Lebensm.*, 1937, **73**, 20.

⁵ S. M. Strepkov, *Biochem. Z.*, 1937, **290**, 91.

⁶ P. A. Shaffer and R. D. Williams, *J. Biol. Chem.*, 1935, **111**, 707.

⁷ C. R. Marshall and A. G. Norman, *Analyst*, 1938, **63**, 315.

⁸ M. Somogyi, *J. Biol. Chem.*, 1937, **117**, 771.

⁹ T. F. Nicholson, *Biochem. J.*, 1936, **30**, 1804.

¹⁰ F. Rappaport and I. Reifer, *Mikrochim. Acta*, 1938, **2**, 273.

Fructose, but not glucose, sucrose, maltose, or lactose, gives a black colour when heated with sulphur and glycerol containing lead acetate,¹¹ and the purple colour produced by warming fructose with skatole and hydrochloric acid¹² affords a selective colorimetric determination.

Starch.—This has been determined hitherto by iodine methods of limited application, or by applying reduction or other methods to the products of hydrolysis. In a rapid iodine method, for which high selectivity and general applicability are claimed, a dilute alkaline solution of the starch is neutralised, and the starch-iodine complex, precipitated by potassium acetate or alcohol under specified conditions, is weighed.¹³ In a modification, starch can be separated almost quantitatively from dextrin.¹⁴

9. MICRO-ANALYSIS.

The development of micro-methods in organic and inorganic analysis during the past year has proceeded over such a wide field that any attempt to cover the subject within the space available in this Report is impossible. Attention will be directed therefore to subjects thought to be of general interest. Foremost in this sense are developments in technique.

The development of qualitative analysis for the rarer elements on the micro-gram scale mentioned in the last Report has been continued,¹ the methods of A. A. Noyes and W. C. Bray² serving as a basis for the work. Most of the operations are carried out in micro-cones of 0.5 c.mm. capacity under observation with a low-power microscope. A screw clamp for closing the cones allows pressure digestions to be performed without loss, and the settling and coagulation of precipitates are accelerated by means of a buzzer clamped firmly to the stand holding the cones. In 1 mg. of material, 5 μ g. of arsenic, germanium, or selenium can be detected in the presence of 500 μ g. of the other two elements, whilst 10 μ g. of any alkali ion may be detected and determined in the presence of not more than 500 μ g. of the others. Osmium and ruthenium can be detected separately in mixtures having ratios Os : Ru varying from

¹¹ E. V. Zmaczynski, *J. Gen. Chem. Russia*, 1937, **7**, 2861.

¹² R. C. Jordan and I. Pryde, *Biochem. J.*, 1938, **32**, 272.

¹³ J. J. Chinoy, F. W. Edwards, and H. R. Nanji, *Analyst*, 1934, **59**, 673.

¹⁴ F. W. Edwards, H. R. Nanji, and W. R. Chanmugam, *ibid.*, 1938, **63**, 697.

¹ A. A. Benedetti-Pichler *et al.*, *Ind. Eng. Chem. (Anal.)*, 1937, **9**, 483, 589; *ibid.*, 1938, **10**, 107; *Mikrochem.*, 1938, **24**, 16.

² "A System of Qualitative Analysis of the Rare Elements," Macmillan and Co., New York, 1927.

1 : 100 to 100 : 1. Suitable confirmatory tests for these elements have also been devised.

The detection and determination of the precious metals in very small quantities have received attention. A micro-titration method for platinum in silver cupellation beads containing also gold and other platinum metals and, possibly, lead and copper, involves solution of the metals as chlorides followed by reduction with stannous bromide. Precipitated gold is filtered off and the bivalent platinum titrated with standard sodium diethyldithiocarbamate solution in the presence of benzene. The end-point is indicated by discharge of colour in the aqueous phase. The benzene solution of the compound of bromine, platinum, and diethyldithiocarbamate left after titration changes in colour from orange to olive-green in direct sunlight, a reaction characteristic of platinum.³

Another interesting method for the recovery of 0.01 mg. of gold or 1.0 mg. of silver from 40 l. of water is described.⁴ Mercuric chloride solution is added to a large volume of the gold-silver solution, and a fine cloud of mercury and mercurous chloride is produced by reduction with magnesium and sulphuric acid. The cloud settles and takes with it all the gold and silver in solution or colloiddally dispersed; these two metals are then recovered from the precipitate by a cupellation process. Sea water, mine water, and ore-leach solutions have been thus tested.

Methods for the analysis of 1 mg. samples, suitable for investigations on the heterogeneity of alloys, metallic diffusion, and composition of surface layers have been devised.⁵ A. Glazunov has employed anodic dissolution⁶ in a chemical examination of the macro-structure of alloys. A piece of filter-paper soaked in a suitable reagent is placed between the metal to be examined and an aluminium cathode. When the metal is connected to the anode, a small quantity passes into solution in the reagent and is identified by the characteristic colour produced.

A method for the colorimetric determination of zinc (0.05—2 mg.) in soils⁷ depends on separation of zinc from interfering elements as sulphide, which is then dissolved in hydrochloric acid and precipitated with 5-nitroquinaldinic acid. Dissolution of the precipitate in stannous chloride and hydrochloric acid gives an orange-coloured solution suitable for photo-electric comparison.

³ W. B. Pollard, *Bull. Inst. Min. Met.*, 1938, Nos. 400 and 406.

⁴ W. E. Caldwell and K. N. McLeod, *Ind. Eng. Chem. (Anal.)*, 1937, **9**, 530.

⁵ A. Portevin and A. Leroy, *Compt. rend.*, 1938, **206**, 518.

⁶ *Österr. Chem.-Ztg.*, 1938, **41**, 217.

⁷ W. L. Lott, *Ind. Eng. Chem. (Anal.)*, 1938, **10**, 335.

The micro-analytical determination of elements present in small quantities in rocks (0.01—0.02%) has been reviewed at length.⁸

Numerous workers have extended and refined the use of many known reagents. Among the new reagents reported is the complex salt $[\text{Fe}^{\text{II}}(2:2'\text{-dipyridyl})_3]\text{SO}_4$, which gives characteristic micro-crystalline precipitates with many anions: *e.g.*, I^- (1 $\mu\text{g.}$), CNS^- (0.2 $\mu\text{g.}$), VO_3' , $\text{Cr}_2\text{O}_7''$, MoO_4'' , etc.⁹

In organic elementary analysis attention has been directed to improvements in the design of automatic combustion furnaces,¹⁰ and to purification of the gas supplied to the combustion tube by passage through a pre-heater made of copper tubing.¹¹ Modifications in the tube filling for carbon and hydrogen determinations have been suggested; copper oxide containing copper, lead, chromium, manganese, and silver in the atomic ratios 12 : 3 : 3 : 1 : 1 is recommended as an oxidation catalyst,¹² and silver deposited electrolytically in the form of closely woven clusters of crystals is preferred to silver wire in the ordinary Pregl method.¹³ Other modifications designed for the more convenient and exact combustion of volatile and easily sublimed substances have also been described.¹⁴ After combustion, the carbon dioxide may be determined by titration with standard baryta,¹⁵ or the water formed may be absorbed in cinnamoyl chloride at 65°, and the liberated hydrogen chloride caught in water and titrated with 0.02N-borax.¹⁶

The direct determination of oxygen by the ter Meulen destructive hydrogenation process has undergone extensive improvement. It can now be applied with reasonable accuracy to most organic compounds, with the possible exception of sugars which have a high oxygen content and produce a voluminous deposit of carbon in the combustion tube: results with these substances are often low.¹⁷ Various hydrogenation catalysts have been used; the best appear to be nickel chromite and nickel-thoria. Both of these are unaffected by sulphur, and it is suggested that the former could be made resistant to halogens also.¹⁸ Before hydrogenation with the latter, the vaporised substance may be cracked over platinised silica,¹⁹

⁸ F. Hecht, *Z. anal. Chem.*, 1937, **110**, 385.

⁹ N. S. Poluektov and V. A. Nazarenko, *J. Appl. Chem. Russia*, 1937, **10**, 2105.

¹⁰ L. T. Hallett, *Ind. Eng. Chem. (Anal.)*, 1938, **10**, 101.

¹¹ W. MacNevin and H. S. Clark, *ibid.*, p. 338.

¹² H. Reihlen, *Mikrochem.*, 1938, **23**, 285.

¹³ W. MacNevin, *Ind. Eng. Chem. (Anal.)*, 1938, **10**, 341.

¹⁴ A. Elek, *ibid.*, p. 51.

¹⁵ R. B. Schmidt and J. B. Niederl, *Mikrochem.*, 1938, **24**, 59.

¹⁶ C. J. van Nieuwenburg, *Mikrochim. Acta*, 1937, **1**, 71.

¹⁷ W. R. Kirner, *Ind. Eng. Chem. (Anal.)*, 1937, **9**, 535.

¹⁸ P. Goodloe and J. C. W. Frazer, *ibid.*, p. 223.

¹⁹ J. Unterzaucher and K. Bürger, *Ber.*, 1937, **70**, 1392.

and halogens removed by passage over heated silver and lime.²⁰ After hydrogenation, the water formed may be absorbed in anhydrous calcium sulphate¹⁷ and weighed, or else absorbed in naphthyl-phosphoryl²¹ or cinnamoyl²² chloride and the liberated hydrogen chloride titrated. If the substance contains nitrogen, the gases leaving the tube often contain ammonia, in which case the water must be absorbed in anhydrous lime.²⁰

Attention is directed to the possibility of errors arising in the micro-Dumas determination of nitrogen through contamination of the final volume of nitrogen with methane,²³ and it is suggested that results by this method should be checked by an alternative procedure. The combustion of volatile substances is simplified by using a U-shaped capillary tube to hold the weighed material. This is centrifuged after filling and before sealing, and avoids the necessity for using potassium chlorate in the Pregl straight weighing tube.²⁴

Acceleration of oxidation in the Kjeldahl digestion with hot concentrated sulphuric acid has been examined.²⁵ Most rapid oxidation is achieved by passage of chlorine through the liquid in the presence of selenium dioxide.

A modification of the Pregl combustion tube for the determination of halogens has been described.²⁶ The necessity for drying the tube before analysis, and waiting for it to cool before the combustion products are washed out after analysis, may be avoided. A very rapid halogen determination may be carried out on materials containing no nitrogen.²⁷ Hydrogenation over a nickel-chromium catalyst liberates the halogen as the corresponding hydride, which may then be absorbed in water and titrated directly with sodium hydroxide or borate, methyl-red or methyl-orange being the indicator.

For the determination of sulphur, the combustion or other destructive oxidation of the material may be followed by titration of the sulphate ion with 0.01N-barium chloride under carefully controlled conditions with sodium rhodizonate as indicator.²⁸ In the Pregl method, transference of the barium sulphate from the precipitation vessel, and the difficulty of removing adherent precipitate may be avoided if precipitation is carried out in a small weighed crucible.

²⁰ J. Unterzaucher and K. Bürger, *Ber.*, 1938, **71**, 429.

²¹ J. Lindner and H. E. Wirth, *Ber.*, 1937, **70**, 1035.

²² A. Lacourt, *Bull. Soc. chim. Belg.*, 1937, **46**, 428.

²³ H. J. Ravenswaay and A. Schweizer, *Rec. Trav. chim.*, 1938, **57**, 688.

²⁴ V. A. Aluise, *Ind. Eng. Chem. (Anal.)*, 1938, **10**, 56.

²⁵ J. Milbauer, *Chem. Obzor*, 1937, **12**, 17.

²⁶ L. T. Hallett, *Ind. Eng. Chem. (Anal.)*, 1938, **10**, 111.

²⁷ A. Lacourt, *Mikrochem.*, 1938, **23**, 308.

²⁸ E. Abrahameczik and F. Blümel, *Mikrochim. Acta*, 1937, **1**, 354.

After precipitation is complete, the mother-liquor is removed through a small, weighed filter stick, the precipitate washed, and the wash liquid removed in the same manner. Crucible, filter stick, and precipitate can then be dried and weighed.²⁹

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H. K. WHALLEY.

²⁹ W. Saschek, *Ind. Eng. Chem. (Anal.)*, 1937, **9**, 491.

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TABLE OF ABBREVIATIONS EMPLOYED IN THE REFERENCES.

<i>Abbreviated Title.</i>	FULL TITLE.
<i>A.</i>	British Chemical Abstracts (Section A).
<i>Acta Med. Scand.</i>	Acta Medica Scandinavica.
<i>Act. sci. ind.</i>	Actualités scientifiques et industrielles.
<i>Amer. J. Physiol.</i>	American Journal of Physiology.
<i>Amer. J. Publ. Health</i>	American Journal of Public Health and the Nation's Health.
<i>Amer. J. Roentgenol.</i>	The American Journal of Roentgenology and Radium Therapy.
<i>Amer. J. Sci.</i>	American Journal of Science.
<i>Amer. Min.</i>	American Mineralogist.
<i>Anal. Fis. Quím.</i>	Anales de la Sociedad Española Física y Química.
<i>Analyst</i>	The Analyst.
<i>Angew. Chem.</i>	Angewandte Chemie (formerly Zeitschrift für angewandte Chemie).
<i>Annalen</i>	Justus Liebig's Annalen der Chemie.
<i>Ann. Bot.</i>	Annals of Botany.
<i>Ann. Chim.</i>	Annales de Chimie.
<i>Ann. Chim. analyt.</i>	Annales de Chimie analytique et de Chimie appliquée.
<i>Ann. Chim. Phys.</i>	Annales de Chimie et de Physique (now divided: see <i>Ann. Chim.</i> and <i>Ann. Physique</i>).
<i>Ann. Intern. Med.</i>	Annals of Internal Medicine.
<i>Ann. Physik</i>	Annalen der Physik.
<i>Ann. Physique</i>	Annales de Physique.
<i>Ann. Reports</i>	Annual Reports on the Progress of Chemistry.
<i>Ann. Rev. Biochem.</i>	Annual Review of Biochemistry.
<i>Ann. Sect. Platine</i>	Annales du Secteur Platine et des autres Métaux Précieux.
<i>Ann. Sect. Anal. Phys. Chim.</i>	Annales du Secteur d'Analyse physicochimique, Institut de Chimie générale (U.R.S.S.).
<i>Ann. Soc. sci. Bruxelles</i>	Annales de la Société scientifique de Bruxelles.
<i>Arch. Pharm.</i>	Archiv der Pharmazie.
<i>Arch. Sci. biol.</i>	Archives des Sciences biologiques (U.R.S.S.).
<i>Atti R. Accad. Lincei</i>	Atti (Rendiconti) della Reale Accademia Nazionale dei Lincei. Classe di scienze fisiche, matematiche e naturali, Roma.
<i>Ber.</i>	Berichte der deutschen chemischen Gesellschaft
<i>Ber. deut. keram. Ges.</i>	Berichte der deutschen keramischen Gesellschaft.
<i>Biochem. J.</i>	The Biochemical Journal.
<i>Biochem. Z.</i>	Biochemische Zeitschrift.
<i>Brit. J. Exp. Path.</i>	British Journal of Experimental Pathology.
<i>Brit. Med. J.</i>	The British Medical Journal.
<i>Bull. Acad. polonaise</i>	Bulletin internationale de l'Académie polonaise des Sciences et des Lettres.
<i>Bull. Acad. Sci. U.R.S.S.</i>	Bulletin de l'Académie des Sciences de l'Union des Républiques Soviétiques Socialistes.
<i>Bull. Chem. Soc. Japan</i>	Bulletin of the Chemical Society of Japan.
<i>Bull. Exp. Biol. Med.</i>	Bulletin of Experimental and Biological Medicine.
<i>Bull. Inst. Min. Met.</i>	Bulletin of the Institution of Mining and Metallurgy.
<i>Bull. Inst. Pin</i>	Bulletin de l'Institut du Pin.
<i>Bull. Johns Hopkins Hosp.</i>	Bulletin of the Johns Hopkins Hospital.
<i>Bull. Soc. chim.</i>	Bulletin de la Société chimique de France.

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Abbreviated Title.	FULL TITLE.
<i>Bull. Soc. chim. Belg.</i>	Bulletin de la Société chimique de Belgique.
<i>Bull. Soc. Chim. biol.</i>	Bulletin de la Société de Chimie biologique.
<i>Bur. Stand. J. Res.</i>	Bureau of Standards Journal of Research (now Journal of Research of the National Bureau of Standards).
<i>Canadian J. Res.</i>	Canadian Journal of Research.
<i>Canadian Med. Assoc. J.</i>	The Canadian Medical Association Journal.
<i>Cereal Chem.</i>	Cereal Chemistry.
<i>Chem. and Ind.</i>	Chemistry and Industry.
<i>Chem. Erde</i>	Chemie der Erde.
<i>Chem. Fabr.</i>	Die Chemische Fabrik.
<i>Chem. News</i>	The Chemical News (now discontinued).
<i>Chem. Obzor</i>	Chemický Obzor.
<i>Chem. Reviews</i>	Chemical Reviews.
<i>Chem. Weekblad</i>	Chemisch Weekblad.
<i>Chem. Zentr.</i>	Chemisches Zentralblatt.
<i>Chim. et Ind.</i>	Chimie et Industrie.
<i>Chim. e l'Ind.</i>	La Chimica e l'Industria.
<i>Chinese J. Physics</i>	Chinese Journal of Physics.
<i>Coll. Czech. Chem. Comm.</i>	Collection of Czechoslovak Chemical Communications.
<i>Compt. rend.</i>	Comptes rendus hebdomadaires des Séances de l'Académie des Sciences.
<i>Compt. rend. Acad. Sci. U.R.S.S.</i>	Comptes rendus de l'Académie des Sciences de l'Union des Républiques Soviétiques Socialistes.
<i>Compt. rend. Soc. Biol.</i>	Comptes rendus hebdomadaires des Séances de la Société de Biologie.
<i>Compt. rend. Trav. Lab. Carlsberg</i>	Comptes rendus des Travaux du Laboratoire Carlsberg.
<i>Current Sci.</i>	Current Science.
<i>Dansk Tidsskr. Farm.</i>	Dansk Tidsskrift for Farmaci.
<i>Deutsche med. Woch.</i>	Deutsche medizinische Wochenschrift.
<i>Edin. Med. J.</i>	Edinburgh Medical Journal.
<i>Ergebn. Enzymforsch.</i>	Ergebnisse der Enzymforschung.
<i>Ergebn. exakt. Naturwiss.</i>	Ergebnisse der exakten Naturwissenschaften.
<i>Ergebn. Vitamin- u. Hormonforsch.</i>	Ergebnisse der Vitamin- und Hormonforschung.
<i>Fortschr. Min.</i>	Fortschritte der Mineralogie, Kristallographie und Petrographie.
<i>Gazzetta</i>	Gazzetta chimica italiana.
<i>Gen. Electric Rev.</i>	General Electric Review.
<i>Helv. Chim. Acta</i>	Helvetica Chimica Acta.
<i>Helv. Physica Acta</i>	Helvetica Physica Acta.
<i>Ind. Eng. Chem.</i>	Industrial and Engineering Chemistry.
<i>Ind. Eng. Chem. (Anal.)</i>	Industrial and Engineering Chemistry: Analytical Edition.
<i>J.</i>	Journal of the Chemical Society.
<i>J. Agric. Res.</i>	Journal of Agricultural Research.
<i>J. Amer. Ceramic Soc.</i>	Journal of the American Ceramic Society.
<i>J. Amer. Chem. Soc.</i>	Journal of the American Chemical Society.
<i>J. Amer. Med. Assoc.</i>	Journal of the American Medical Association.
<i>J. Amer. Pharm. Assoc.</i>	Journal of the American Pharmaceutical Association.
<i>J. Appl. Chem. Russia</i>	Journal of Applied Chemistry, Russia (Zhurnal prikladnoi Khimii).
<i>J. Appl. Physics.</i>	Journal of Applied Physics (U.S.S.R.).
<i>J. Biol. Chem.</i>	Journal of Biological Chemistry.
<i>J. Biol. Chem. Sci. Proc.</i>	Scientific Proceedings of the American Society of Biological Chemists [bound with <i>J. Biol. Chem.</i>].
<i>J. Chem. Physics</i>	The Journal of Chemical Physics.
<i>J. Chim. physique</i>	Journal de Chimie physique.
<i>J. Chinese Chem. Soc.</i>	Journal of the Chinese Chemical Society.
<i>J. Clin. Invest.</i>	The Journal of Clinical Investigation.

Abbreviated Title.	FULL TITLE.
<i>J. Electrochem. Assoc. Japan</i>	Journal of the Electrochemical Association of Japan.
<i>J. Fac. Sci. Hokkaido Imp. Univ.</i>	Journal of the Faculty of Science, Hokkaido Imperial University.
<i>J. Gen. Chem. Russia</i>	Journal of General Chemistry (U.S.S.R.) (formerly chemical part of the Journal of the Physical and Chemical Society of Russia).
<i>J. Immunol.</i>	The Journal of Immunology.
<i>J. Indian Chem. Soc.</i>	Quarterly Journal of the Indian Chemical Society.
<i>J. Ind. Eng. Chem.</i>	Journal of Industrial and Engineering Chemistry [now Industrial and Engineering Chemistry].
<i>J. Indian Inst. Sci.</i>	Journal of the Indian Institute of Science.
<i>J. Inst. Brew.</i>	Journal of the Institute of Brewing.
<i>J. Inst. Metals</i>	Journal of the Institute of Metals.
<i>J. Iron Steel Inst.</i>	Journal of the Iron and Steel Institute.
<i>J. Nutrition</i>	Journal of Nutrition.
<i>J. Org. Chem.</i>	The Journal of Organic Chemistry.
<i>J. Pharm. Chim.</i>	Journal de Pharmacie et de Chimie.
<i>J. Pharm. Exp. Ther.</i>	Journal of Pharmacology and Experimental Therapeutics.
<i>J. Pharm. Soc. Japan</i>	Journal of the Pharmaceutical Society of Japan (Yakugakuzasshi).
<i>J. Phys. Chem. Russia</i>	Journal of Physical Chemistry, Russia (Zhurnal Fizitscheskoi Khimii).
<i>J. Phys. Radium</i>	Journal de Physique et le Radium.
<i>J. Physical Chem.</i>	The Journal of Physical Chemistry.
<i>J. Physiol.</i>	Journal of Physiology.
<i>J. pr. Chem.</i>	Journal für praktische Chemie.
<i>J. Proc. Roy. Soc. N.S.W.</i>	Journal and Proceedings of the Royal Society of New South Wales.
<i>J. Res. Nat. Bur. Stand.</i>	Journal of Research of the National Bureau of Standards (formerly Bureau of Standards Journal of Research).
<i>J. Sci. Instr.</i>	Journal of Scientific Instruments.
<i>J. Soc. Chem. Ind.</i>	Journal of the Society of Chemical Industry.
<i>J. Text. Inst.</i>	Journal of the Textile Institute.
<i>Kgl. Danske Videnskab. Selskab</i>	Kongelige Danske Videnskabernes Selskab, Matematisk-fysiske Meddelelser.
<i>Klin. Woch.</i>	Klinische Wochenschrift.
<i>Kolloid-Z.</i>	Kolloid-Zeitschrift.
<i>Lancet</i>	The Lancet.
<i>Mem. Coll. Agric. Kyoto</i>	Memoirs of the College of Agriculture, Kyoto Imperial University.
<i>Mem. Inst. Chem. Ukrain. Acad. Sci.</i>	Memoirs of the Institute of Chemistry, Ukrainian Academy of Sciences.
<i>Mem. Manchester Lit. Phil. Soc.</i>	Memoirs and Proceedings of the Manchester Literary and Philosophical Society.
<i>Mem. R. Accad. Ital.</i>	Memorie della reale Accademia d'Italia. Classe di Scienze fisiche, matematiche e naturali.
<i>Mem. Ryojun Coll. Eng.</i>	Memoirs of the Ryojun College of Engineering.
<i>Metallw.</i>	Metallwirtschaft, Metallwissenschaft, Metalltechnik.
<i>Mikrochem.</i>	Mikrochemie.
<i>Mikrochim. Acta</i>	Mikrochimica Acta.
<i>Min. Mag.</i>	Mineralogical Magazine and Journal of the Mineralogical Society.
<i>Monatsh.</i>	Monatshefte für Chemie und verwandte Teile anderer Wissenschaften.
<i>Naturwiss.</i>	Die Naturwissenschaften.
<i>Nederl. Tijds. Natuurk.</i>	Nederlandsch Tijdschrift voor Natuurkunde.
<i>Neues Jahrb. Min.</i>	Neues Jahrbuch für Mineralogie, Kristallographie und Petrographie.
<i>New England J. Med.</i>	New England Journal of Medicine.
<i>New Phytol.</i>	New Phytologist.

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Abbreviated Title.	FULL TITLE.
<i>Norges Tekn. Høiskole Ahandl.</i>	Norges Tekniske Høiskole Avhandling.
<i>Norske Vidensk. Skr.</i>	Skrifter utgitt av det Norske Videnskaps-Akademi i Oslo.
<i>Nuovo Cim.</i>	Nuovo Cimento.
<i>Nutrit. Abs. Rev.</i>	Nutrition Abstracts and Reviews.
<i>Österr. Chem.-Ztg.</i>	Österreichische Chemiker-Zeitung.
<i>Pharm. Weekblad</i>	Pharmaceutisch Weekblad.
<i>Phil. Mag.</i>	Philosophical Magazine (The London, Edinburgh and Dublin).
<i>Phil. Trans.</i>	Philosophical Transactions of the Royal Society.
<i>Physical Rev.</i>	Physical Review.
<i>Physikal. Z.</i>	Physikalische Zeitschrift.
<i>Physikal. Z. Sowjetunion</i>	Physikalische Zeitschrift der Sowjetunion.
<i>Physiol. Rev.</i>	Physiological Reviews.
<i>Polska Gaz. lekarska</i>	Polska Gazeta lekarska.
<i>Proc. Camb. Phil. Soc.</i>	Proceedings of the Cambridge Philosophical Society.
<i>Proc. Geol. Assoc.</i>	Proceedings of the Geologists' Association.
<i>Proc. Indian Acad. Sci.</i>	Proceedings of the Indian Academy of Science.
<i>Proc. K. Akad. Wetensch. Amsterdam</i>	Koninklijke Akademie van Wetenschappen te Amsterdam (Proceedings, English version).
<i>Proc. Nat. Acad. Sci.</i>	Proceedings of the National Academy of Sciences.
<i>Proc. Phys. Math. Soc. Japan</i>	Proceedings of the Physico-mathematical Society of Japan.
<i>Proc. Physical Soc.</i>	Proceedings of the Physical Society of London.
<i>Proc. Roy. Inst.</i>	Proceedings of the Royal Institute of Great Britain.
<i>Proc. Roy. Soc.</i>	Proceedings of the Royal Society.
<i>Proc. Roy. Soc. Edinburgh</i>	Proceedings of the Royal Society of Edinburgh.
<i>Proc. Roy. Soc. Medicine</i>	Proceedings of the Royal Society of Medicine.
<i>Proc. Soc. Exp. Biol. Med.</i>	Proceedings of the Society for Experimental Biology and Medicine.
<i>Proc. Staff Meetings Mayo Clinic</i>	Proceedings of the Staff Meetings of the Mayo Clinic.
<i>Quart. J. Pharm.</i>	Quarterly Journal of Pharmacy and Pharmacology.
<i>Rec. Trav. chim.</i>	Recueil des Travaux chimiques des Pays-Bas et de la Belgique.
<i>Rev. Mod. Physics</i>	Reviews of Modern Physics.
<i>Rev. Sci. Instr.</i>	Review of Scientific Instruments.
<i>Ric. sci.</i>	Ricerca scientifica.
<i>Schweiz. med. Woch.</i>	Schweizerische medizinische Wochenschrift.
<i>Sci. J. Roy. Coll. Sci.</i>	The Scientific Journal of the Royal College of Science.
<i>Sci. Papers Inst. Phys. Chem. Res. Tokyo</i>	Scientific Papers of the Institute of Physical and Chemical Research, Tokyo.
<i>Sitzungsber. Ges. Beförd. Naturwiss. Marburg</i>	Sitzungsberichte der Gesellschaft zur Beförderung der gesamten Naturwissenschaften zu Marburg.
<i>Skand. Arch. Physiol.</i>	Skandinavisk Archiv för Fysiologi.
<i>Suomen Kem.</i>	Suomen Kemistilehti (Acta Chemica Fennica).
<i>Tids. Kjemi</i>	Tidsskrift for Kjemi og Bergvesen.
<i>Trans. Amer. Soc. Metals</i>	Transactions of the American Society of Metals.
<i>Trans. Electrochem. Soc.</i>	Transactions of the Electrochemical Society.
<i>Trans. Faraday Soc.</i>	Transactions of the Faraday Society.
<i>Trans. Roy. Soc. Canada</i>	Transactions of the Royal Society of Canada.
<i>Trans. Roy. Soc. Trop. Med. Hyg.</i>	Transactions of the Royal Society of Tropical Medicine and Hygiene.
<i>Trans. State Inst. Appl. Chem. U.S.S.R.</i>	Transactions of the State Institute of Applied Chemistry (U.S.S.R.).
<i>Trans. Wisconsin Acad. Sci.</i>	Transactions of the Wisconsin Academy of Sciences, Arts and Letters.
<i>Z. anal. Chem.</i>	Zeitschrift für analytische Chemie.
<i>Z. angew. Chem.</i>	Zeitschrift für angewandte Chemie (now Angewandte Chemie).

Abbreviated Title.	FULL TITLE.
<i>Z. angew. Min.</i> . . .	Zeitschrift für angewandte Mineralogie.
<i>Z. anorg. Chem.</i> . . .	Zeitschrift für anorganische und allgemeine Chemie.
<i>Z. Elektrochem.</i> . . .	Zeitschrift für Elektrochemie (und angewandte physikalische Chemie).
<i>Z. ges. exp. Med.</i> . . .	Zeitschrift für die gesammte experimentelle Medizin zugleich Fortsetzung der Zeitschrift für experimentelle Pathologie und Therapie.
<i>Z. Krist.</i> . . .	Zeitschrift für Kristallographie.
<i>Z. Metallk.</i> . . .	Zeitschrift für Metallkunde.
<i>Z. Physik</i> . . .	Zeitschrift für Physik.
<i>Z. physikal. Chem.</i> . . .	Zeitschrift für physikalische Chemie, Stöchiometrie und Verwandtschaftslehre.
<i>Z. physiol. Chem.</i> . . .	Hoppe-Seyler's Zeitschrift für physiologische Chemie.
<i>Z. Unters. Lebensm.</i> . . .	Zeitschrift für Untersuchung der Lebensmittel.
<i>Z. Vitaminforschung</i> . . .	Zeitschrift für Vitaminforschung.
<i>Zavod. Lab.</i> . . .	Zavodskaja Laboratorija.
<i>Zentr. Min.</i> . . .	Zentralblatt für Mineralogie, Geologie und Paläontologie.

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